71

Muscle attenuation and sarcopaenia in gastric and oesophageal cancers

Katherine Geddes[1], Hannah Rouse[1], Sue-Anne McLachlan[2, 1], Vijaya Sundararajan[2], Melissa Moore[2, 1]

1. St Vincent's Hospital, Fitzroy, VIC, Australia

2. The University of Melbourne, Parkville, Victoria, Australia

Background: Body composition measures of sarcopaenia (low muscle mass) and low muscle attenuation (LMA) have been independently associated with poor prognosis in cancer. Muscle attenuation(MA) refers to the degree of fat infiltration within skeletal muscle. LMA comprises higher fat infiltration equating to lower muscle quality. We aimed to explore body composition in our population with gastric and oesophageal cancers undertaking neoadjuvant and palliative treatments.

Methods: Patients diagnosed with gastric or oesophageal cancers with digital imaging that received chemotherapy between 2010 and 2014 at St Vincent's Hospital were included. Our primary aim was to quantify and describe MA in this population. CT-based body composition analysis by Slice-O-Matic software measured the muscle cross-sectional area and density in Hounsfield units(HU) at diagnosis and after 3 months of treatment.

Results: Primary analysis included 32 patients. 72%(N=23) were sarcopaenic at diagnosis, three-quarters of those patients lost further muscle mass throughout chemotherapy. Median MA at baseline was 37HU(range 24-50; SD 8). Median MA post chemotherapy was 26HU(15-37, SD 5.7). 60% had LMA at baseline, 64% lost MA at 3 months, 14% gained. All patients had LMA after chemotherapy, including all of those with normal MA at baseline. One third reduced their MA by more than 40%, almost half had a reduction between 10 & 39%. 44% had normal range body mass index(BMI) at diagnosis, 25% underweight, 25% overweight and 6% obese. 100% of those underweight were also sarcopaenic, 72% of normal and 63% of overweight. MA was varied across BMI categories. 68% of those with LMA were also sarcopaenic. Survival data will follow.

CONCLUSION: Most patients with gastric or oesophageal cancers have LMA at diagnosis regardless of stage. For those with normal MA, all will become low during treatment. MA does not correlate with BMI. The prognostic significance of LMA and sarcopaenia warrant further investigation to develop tailored interventions to improve cancer outcomes moving forward.

72

Yttrium-90 radioembolisation in unresectable cholangiocarcinoma – a tertiary centre experience

Aaron C Tan[1], Kathy Willowson[2], Dale Bailey[3], Elizabeth Bernard[3], Babak Sanadgol[4], Richard Maher[4], Stephen Clarke[1], Nick Pavlakis[1]

1. Department of Medical Oncology, Royal North Shore Hospital, St Leonards, NSW, Australia

2. Institute of Medical Physics, University of Sydney, Sydney, NSW, Australia

3. Department of Nuclear Medicine, Royal North Shore Hospital, St Leonards, NSW, Australia

4. Department of Radiology, Royal North Shore Hospital, St Leonards, NSW, Australia

Introduction:

Advanced intra-hepatic cholangiocarcinoma remains a malignancy with poor prognosis and a median survival of less than 12 months. There are no recognised standard treatment options following systemic chemotherapy with platinum-gemcitabine. Selective internal radiation therapy (SIRT) with Yttrium-90 radioembolisation represents a potential locoregional treatment option in cases with liver limited/dominant disease.

Methods:

A retrospective analysis was conducted of patients receiving resin-based Yttrium-90 radioembolisation for unresectable intra-hepatic cholangiocarcinoma between September 2013 and May 2017 at Royal North Shore Hospital, Sydney. In all cases, decision for SIRT was made in the multidisciplinary team meeting. Tumour response was assessed on follow-up FDG-PET scan and computed tomography (CT) imaging. Response of individual lesions to therapy was investigated correlating SUV uptake on baseline and follow-up FDG-PET. Progression-free survival (PFS) and overall survival (OS) was determined from the date of first Yttrium-90 procedure.

Results:

Ten patients underwent 12 Yttrium-90 procedures. Two patients received two treatments; one to separate lobes of the liver and one repeated treatment. Six patients had extra-hepatic metastases. All ten patients had received prior systemic chemotherapy, nine with platinum-gemcitabine doublet chemotherapy and one with gemcitabine monotherapy. Nine patients had multifocal hepatic disease with eight having bilobar involvement. With a median follow-up of 156 days (range 42-535 days), median hepatic PFS was 79 days and median extra-hepatic PFS was 175 days. Median OS was 496 days. On follow-up FDG-PET (median 52 days following procedure) of 10 Yttrium-90 procedures, there were four with partial response, five with stable disease and one with progressive disease (PD). Of the patients with partial response, two had individual lesions with complete response on FDG-PET. No

grade 3 or 4 toxicities were reported. There was one death within 90 days of Yttrium-90 procedure due to PD. Seven patients underwent subsequent lines of systemic therapy following Yttrium-90 treatment. One patient with a solitary liver lesion underwent subsequent transarterial chemoembolisation followed by resection and remains disease free at 434 days of follow-up.

Conclusion:

This case series of highly selected patients highlights Yttrium-90 radioembolisation as a safe and promising treatment option for unresectable cholangiocarcinoma after progression on standard first-line chemotherapy.

73

Outcomes of neoadjuvant concurrent chemoradiotherapy in borderline resectable pancreatic cancer at a Sydney tertiary referral centre.

William Fox[1], Peter Grimison[1], Regina Tse[1, 2], Philip Beale[1, 2], George Hruby[1, 2], Nazmeen Shameem[1], Charbel Sandroussi[1]

1. The Chris O'Brien Lifehouse, Sydney, NSW, Australia

2. Concord Cancer Centre, Sydney, NSW, Australia

Introduction: Neoadjuvant therapy prior to surgery may increase the likelihood of complete (R0) resection for borderline resectable pancreatic cancer, but the optimal protocol is unknown[1,2,3]. The aim of this retrospective review was to determine the feasibility, tolerability and outcomes of neoadjuvant concurrent chemoradiotherapy (NCRT) at Royal Prince Alfred Hospital and Chris O`Brien Lifehouse.

Methods: We identified patients with biopsy-proven borderline resectable pancreatic adenocarcinoma that commenced NCRT between January 2009 and January 2016. The primary endpoint was rate of R0 surgical resection. Secondary endpoints included feasibility, tolerability, progression-free-survival (PFS), overall survival (OS).

Results: We identified 12 patients. Median age was 61 years (range 51-72). All received radiotherapy (50.4 Gy in 28 fractions) with concurrent chemotherapy (infusional 5-fluorouracil 1575 mg/m^2/week or capecitabine 800-825 mg/m^2 bd 5 days/week). 12 (100%) completed chemoradiotherapy, with only G3/4 non-haematologic toxicity of G3 nausea in 1 patient. 3 (25%) achieved R0 surgical resection, 3 (25%) achieved R1 resection, 3 (25%) were not sufficiently downstaged for surgery, 3 (25%) had progressive disease. The 2-year survival is 17% (95% CI 3-41%) and 1 patient remains alive at 7 years. Median (IQR) PFS and OS are 5 (2-12) months and 21 (12-22) months respectively. There was a trend to better PFS and OS for patients who underwent resection (Figures).

Conclusion: NCRT is well tolerated however rates of R0 resection (25%) and long-term survival are low. A contemporary paradigm would be up-front chemotherapy with more potent agents (Gemcitabine and Nab-paclitaxel or FOLFIRINOX) followed by re-staging then NCRT then surgery however further investigation is warranted.

1. Liu Y, Gou SM, Tang Y et al. Clinical effectiveness of preoperative neoadjuvant chemotherapy for patients with borderline resectable pancreatic cancer: an updated metaanalysis. Current Science 2016; 110 (4)
2. Nelson AR, Bose D. Impact of neoadjuvant therapy on the surgical management of pancreatic cancer: a literature review. Transl Cancer Res 2015;4(6):641-652
3. Itchins M, Arena J, Pavlakis N et al. Pattern of Care and Survival of Pancreatic Ductal Adenocarcinoma in a Multi-Disciplinary High-Volume Centre. J Pancreat Res Disord Ther 2017;1(1):00005

74

NAB-PACLITAXEL + GEMCITABINE FOR ADVANCED PANCREATIC CANCER - A RETROSPECTIVE AUDIT OF DOSE INTENSITY, TOXICITY AND EFFICACY

Andrew Mant[1], Rachel Wong[1], Margaret Lee[1]

1. Eastern Health, Box Hill, VICTORIA, Australia

Background: The MPACT study established the role of nab-paclitaxel/gemcitabine (nab-P/gem) as first-line treatment for advanced pancreatic cancer. Treatment was administered D1/8/15 q28d, however most trial patients required dose reductions and/or delay.[1] An exploratory analysis suggested dosing modifications did not compromise efficacy.[1] It has been suggested that a week-on week-off (WOWO = D1/15 q28d) regimen is potentially less toxic but no less efficacious than the standard regimen.[2]

At Eastern Health, patients intolerant of the D1/8/15 regimen are often switched to WOWO. This audit aims to assess the characteristics and outcomes of these two groups.

Methods: This is a retrospective audit of patients with advanced pancreatic cancer treated with nab-P/gem between February 2014 and February 2017. Patient demographics, disease characteristics, treatment, toxicity and survival outcomes were recorded.

Results: Thirty patients were identified; mean age was 65 years; 60% were male. Nineteen patients (63%) were maintained on standard-nab-P/gem. Of these patients, 26% required a dose reduction and 74% a dose delay or omission. Eleven patients (37%) were switched to WOWO. Reasons for switching were: haematological toxicity 37%; peripheral neuropathy 27% and fatigue 27%. The median number of cycles received was 4.3 for the standard-group versus 6.7 for the WOWO-group. Cessation of chemotherapy due to toxicity was similar in both groups, however more patients in the WOWO-group ceased due to progressive disease (45% versus 37%, p=NS). Progression-free survival was 9.5 months in the WOWO-group, versus 7.8 months in the standard-group (HR 0.72, 95% CI 0.31-1.65, p=0.42). Overall survival was 11.5 months in the WOWO-group, versus 11.3 months in the standard-group (HR 0.86, 95% CI 0.32-2.34, p=0.77).

Conclusion: This study suggests WOWO-nab-P/gem may be as effective yet potentially less toxic than standard-nab-P/gem for advanced pancreatic cancer.

1. Scheithauer W, Ramanathan RK, Moore M, et al. Dose modification and efficacy of nab-paclitaxel plus gemcitabine vs. gemcitabine for patients with metastatic pancreatic cancer: phase III MPACT trial. J Gastrointest Oncol 2016; 7(3):469-478
2. Krishna K, Blazer AM, Wei L, et al. Modified gemcitabine and nab-paclitaxel in patients with metastatic pancreatic cancer (MPC): A single-institution experience. J Clin Oncol 33, 2015 (suppl 3; abstr 366)

75

Deflexifol (a novel formulation of 5FU): phase 1 dose escalation study of infusional and bolus schedules after failure of standard treatment

Philip Clingan[1], Marie Ranson[2], Daniel Brungs[2], Suzanne Parker [1], Morteza Aghmesheh [3], Madhu Garg [4], Anne Henderson [1], Rebecca Jokela[1], Stephen Ackland[4, 5], Paul De Souza[6]

1. Southern Medical Day Care Centre, Wollongong, NSW, Australia

2. Illawarra Health and Medical Research Institute, University of Wollongong , Wollongong , NSW, Australia

3. Medical Oncology, Illawarra Cancer Care Centre, Wollongong , NSW, Australia

4. Calvary Mater Hospital/ Hunter Medical Research Institute, Newcastle , NSW, Australia

5. University of Newcastle , Newcastle , New South Wales, Australia

6. Medical Oncology, Ingham Institute for Applied Medical Research , Liverpool , NSW, Australia

BACKGROUND: 5-Fluorouracil (5FU) is administered in combination with leucovorin (LV) to enhance clinical activity. However, simultaneous administration is not possible because 5FU and LV are chemically incompatible. Deflexifol, an all in one formulation of 5FU/LV with cyclodextrin (HP-β-CD 100mg/ml, 5-FU 15mg/ml & LV 1mg/ml) at physiological pH, was developed as an alternative.

METHODS: A phase I dose-escalation trial to assess the safety, tolerability, MTD and DLT of Deflexifol given in two schedules has been completed. Secondary objectives included the pharmacokinetic (PK) profile and efficacy outcomes. Cohorts of patients with advanced malignancy after failure of standard treatment received Deflexifol as 46-h infusion Q2W or bolus weekly x6 in a standard 3+3 phase I design with no intra-patient dose escalation from dose level 1: 375mg/m² bolus or 1200mg/m² infusional up to dose level 5: 575mg/m² bolus or 3600mg/m² infusional. PK sampling of 5FU and dihydroFU was conducted on all pts to assess PK variability and adequacy of dosing.

RESULTS: 40 patients (21 infusional, 19 bolus) with breast (7), colorectal (24), other GI (6) & NSCLC (3) received a total 293 doses of Deflexifol. No >grade 1 toxicity was noted at 375-475 mg/m^2 bolus, or at 1200-2400 mg/m^2 infusion. The DLT in bolus schedule was grade 3 diarrhea and myelosuppression at 575 mg/m^2, with no DLT in the infusion schedule at the maximum dose 3600 mg/m^2. The MTD have been established for both treatment arms: bolus 525mg/m²; 46-h infusion 3,600mg/m², with no grade IV toxicity observed. Other grade 3 toxicities were nausea, vomiting, and raised liver function tests. 5FU PK in this mixture is similar to 5FU alone. Encouraging efficacy results were seen in a heavily pretreated patient cohort.

Conclusion: Deflexifol has little toxicity and is effective in bolus and infusion schedules at an increased dosing density than with 5FU and LV infused separately. No grade IV toxicity was experienced in either schedule. A phase II study in combination with oxaliplatin is planned.

76

Single institution review of the correlation between the clinical and histopathological staging in newly diagnosed rectal cancer patients in 2015

Padmini Thanayankeezhil[1], David Wyld[1], Matthew Burge[1], Melissa Eastgate[1]

1. Royal Brisbane and Womens hospital, Carseldine, QLD, Australia

Introduction: The management of rectal cancer (RC) requires a multidisciplinary approach. Pre-operative (chemo)radiation is often given to reduce the risk of local recurrence, based on pelvic MRI scan. Given toxicity and cost, tailoring pre-operative therapy to those who need it most is critical. Nodal staging by MRI is reported to lack accuracy. Therefore, we reviewed MRI and histopathologic stage, treatment decisions and their rationale for newly diagnosed non-metastatic RC discussed at the Royal Brisbane colorectal multidisciplinary meeting.

Methods: Clinicopathologic data and the rationale for treatment decisions was retrospectively extracted from electronic medical records. Clinical (C) and histopathologic (P) stages were compared.

RESULTS: Eighty patients were eligible . 24 patients had no preoperative treatment and went for immediate surgery (IS).49 patients had long course chemoradiation (LCCRT).5 patients had short course radiotherapy prior to surgery(SC) . Data regarding the treatments were not available for 2 patients.

In the IS group, C and P staging of N status was concordant in 10 of 26 patients, in the SC group there was no concordance in the 5 patients, and in the LCCRT group, N status was concordant in only 10 of 49 patients, with 31 having been downstaged and only 7 upstaged .

Of the patients who had long course chemoradiation, 7 patients had a grade 0 response to chemotherapy, 15 patients had a grade 1 response, 11 patients had a grade 2 response and 11 patients had a grade 3 response according to pathological grading.

CONCLUSION: Preoperative MRI nodal staging corresponded to the pathologic staging in10 of 24 (50%) patients who went immediately to surgery, which supports the proposition that MRI is not a reliable way to assess nodal status in rectal cancer.

77

Clinical outcomes and emergent circulating tumour (ct)DNA *RAS* mutations and allele fraction for patients with metastatic colorectal cancer (mCRC) treated with panitumumab from the ASPECCT study

Timothy J Price[1, 2], Marc Peeters[2], Mike Boedigheimer[3], Tae Won Kim[4], Peter Gibbs[5], Anne Thomas[6], Kristina Holl[3], Agnes Yong[3], Bruce Bach[3]

1. Queen Elizabeth Hospital, Woodville, SA, Australia

2. Antwerp University Hospital and University of Antwerp, Antwerp, Belgium

3. Amgen Inc., Thousand Oaks, USA

4. Asan Medical Center, University of Ulsan, Seoul, Korea

5. Medical Oncology, Western Hospital and University of Melbourne, Melbourne, Victoria, Australia

6. Leicester Infirmary, Leicester, United Kingdom

Background: ASPECCT was a phase III clinical trial performed in the chemotherapy-refractory third-line mCRC setting (N=1010). This analysis explores the relationship between circulating levels of mutations and clinical outcomes for panitumumab-treated subjects using univariate and multivariate models that treat total mutational load as a continuous measure.

Methods: 238 subjects treated with panitumumab had paired plasma samples at baseline and post-treatment (PT). Samples were analysed for mutations using the Plasma*Select*-R™ 63-gene panel (0.1% limit of detection). The fraction of mutant *RAS* reads was evaluated for association with tumour response (by RECIST) and overall survival using univariate and multivariate Cox proportional hazards models.

Results: 52% of the subjects who were *RAS* wild-type by plasma at baseline never developed a *RAS* mutation. For those with mutant *RAS* ctDNA (KRAS+NRAS) detected at baseline or PT, there was an overall increase in *RAS* mutant DNA fraction at PT compared to baseline. By non-parametric analysis, there was no difference in the distribution of baseline mutant *RAS* fraction between those who achieved stable disease (SD) or those with progression (P = 0.09). There was also no difference in the increase in mutant *RAS* fraction on therapy between subjects with SD or progressive disease (PD). In addition, *RAS* mutation was not required for progression: 48% of subjects with PD had no *RAS* mutant DNA detected.

Conclusions: In this exploratory analysis, baseline plasma mutant *RAS* fraction is an unreliable predictor of subsequent tumour response. Subjects with objective response or SD may have stable or rising levels of mutant *RAS* DNA. Subjects without any detectable *RAS* mutation still experience PD. These findings suggest that detectable plasma ctDNA *RAS* mutations do not necessarily predict response to panitumumab and should be interpreted with caution. Further work is needed to establish clinically relevant and validated thresholds.

78

Impact of primary tumour location (PTL) on response and resection outcomes in patients with metastatic colorectal cancer (mCRC) undergoing first-line treatment

Timothy J Price[1, 2], Marc Peeters[2], Julien Taieb[3], Michael Geissler[4], Fernando Rivera[5], Jean-Luc Canon[6], Reija Koukakis[7], Peter Burdon[8], Salvatore Siena[9]

1. Queen Elizabeth Hospital, Woodville, SA, Australia

2. Antwerp University Hospital and University of Antwerp, Antwerp, Belgium

3. Paris Descartes University, Georges Pompidou European Hospital, Paris, France

4. Cancer Center Esslingen, Esslingen, Germany

5. Hospital Universitario Marqués de Valdecilla, Santander, Spain

6. Service d'Oncologie-Hématologie, Grand Hôpital de Charleroi, Charleroi, Belgium

7. Amgen Inc., Thousand Oaks, USA

8. Biostatistics, AMGEN, Uxbridge, UK

9. Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, and Dipartimento di Oncologia e Emato-Oncologia, Università degli Studi di Milano, Milan, Italy

Background

We retrospectively analysed data from two randomised trials of the EGFRi, panitumumab, to investigate the effects of PTL/treatment on additional response measures and resection outcomes.

Methods

Details of the PRIME (NCT00364013) and PEAK (NCT00819780) studies have previously been reported. Only patients with *RAS* wild-type (WT) mCRC were included. Baseline demographics/disease characteristics were summarised in patients with left (L-SD)- and right-sided disease (R-SD) and the effect of PTL/treatment on resection rates, early tumour shrinkage (ETS) and depth of response (DpR) analysed. PFS and OS were analysed by treatment, PTL, and ETS status.

Results

435/559 patients had L-SD. Patients with L-SD were more likely to have *BRAF* WT tumours (94% vs. 68%) and treatment duration ≥9 months (37% vs. 27%) vs patients with R-SD. More patients with L-SD vs. R-SD underwent resection and experienced ETS; panitumumab was associated with a higher rate of ETS in L-SD but not R-SD. Median DpR was higher in L-SD vs. R-SD overall and with panitumumab. In L-SD, median PFS and OS were prolonged with panitumumab vs. comparator; results for panitumumab were less clear in R-SD. Overall, ETS appeared to be associated with improved survival irrespective of PTL.

Conclusions

Patients with R-SD have worse response and resection outcomes during first-line treatment. ETS is associated with PFS and OS benefits in mCRC, regardless of treatment received or PTL. ETS, DpR, PFS and OS may also be improved with panitumumab vs. comparator treatment in L-SD; results were less clear in R-SD. Overall response rates for R-SD have previously been shown to be higher for anti-EGFR vs. bevacizumab. Intrinsic tumour sensitivity to therapy remains the main determinant of clinical outcome, but ETS might predict a subgroup of patients with R-SD who may achieve improved outcomes with an anti-EGFR/chemotherapy. Patients with R-SD not responding to FOLFOX+panitumumab at 8 weeks may benefit from treatment change.

79

Profiling circulating tumor (ct)DNA mutations after panitumumab treatment in patients with refractory metastatic colorectal cancer (mCRC) from the phase III ASPECCT study

Timothy Price[1, 2], Marc Peeters[2], Mike Boedigheimer[3], Agnes Ang[3], Tae Won Kim[4], Peter Gibbs[5], Anne Thomas[6], Kristina Hool[3], Bruce Bach[3]

1. Queen Elizabeth Hospital, Woodville, SA, Australia

2. Antwerp University Hospital and University of Antwerp, Antwerp, Belgium

3. Amgen Inc., Thousand Oaks, USA

4. Asan Medical Center, University of Ulsan, Seoul, Korea

5. Medical Oncology, Western Hospital and University of Melbourne, Melbourne, Victoria, Australia

6. Leicester Infirmary, Leicester, United Kingdom

Background: ASPECCT was a clinical trial performed in the chemotherapy-refractory third-line mCRC setting (N=1010). This biomarker analysis explores the mutational landscape in panitumumab monotherapy subjects. Analysis of plasma ctDNA at baseline and post-treatment (PT) by NGS provides a snapshot of the main changes in key genes before and after therapy.

Methods: CtDNA collected at baseline and PT was analysed for mutations using the Plasma*Select*-R™ 63-gene panel (0.1% limit of detection). Gain/loss of mutation was defined at the amino acid level. Net change is the sum of mutations gained minus the sum of mutations lost. A single individual could have both net gain and/or net loss of mutations within a single gene.

Results: Significant tumour clonal diversification was observed during therapy. In 238 subjects with paired plasma samples, 29% had multiple mutations in the same gene at baseline and 41% had multiple mutations in the same gene PT. At least 10% of subjects demonstrated an on-therapy acquired mutation in at least one of the following genes: *APC*, *EGFR*, *ALK*, *HER4*, *TP53*, *AR*, *KRAS*, *BRAF*, *PDGFRA*, *STK11, ESR1, FBXWT*, and *KIT* (ordered by frequency). New mutations were noted both inside and outside the EGFR pathway. Unexpectedly, patients with a large decrease in mutant DNA burden after anti-EGFR treatment were also seen. EGFR pathway genes with significant net gain were: *KRAS*, *EGFR*, *NRAS*, *BRAF*, *MAP2K1*, *PIK3CA*, and *AKT1*. Non-EGFR pathway mutations gained included: *APC*, *CDK6*, *SMARCB1*, *FBXW7*, *TERT*, *RB1*, *CTNNB1*, and *IDH1*.

Conclusions: This 63-gene plasma analysis suggests that there are significant dynamic changes in clonal mutational fraction under anti-EGFR selection. Our analysis reveals that increasing global tumour heterogeneity is associated with poorer overall survival. A subset of patients demonstrated an overall decrease in tumour heterogeneity on panitumumab therapy (28%), indicating that under anti-EGFR selective pressure mutational heterogeneity can also decrease.

80

A Retrospective Audit of Outcomes of Carboplatin/Paclitaxel Chemoradiation for Oesophageal Cancer

Rita McMorrow[1], Sarat Chander[2], Michael Ng[3], Rachel Wong[1]

1. Department of Medical Oncology, Eastern Health, Box Hill

2. Department of Radiation Oncology, Peter MacCallum, Box Hill

3. Radiation Oncology Victoria, Ringwood

Background Oesophageal cancer is the eighth most common cancer worldwide. Preoperative chemoradiotherapy (CRT) using carboplatin/paclitaxel improves survival among patients with potentially curable oesophageal or oesophagogastric-junction cancer. This retrospective audit investigated patients treated with neoadjuvant or definitive carboplatin/paclitaxel-based CRT, evaluating survival outcomes and recurrence patterns at our institution.

Methods A retrospective audit was conducted with approval from the Eastern Health ethics committee (QA97-2016). The medical records database was used to identify patients receiving CRT using carboplatin/paclitaxel as defined by the CROSS protocol between May 2014 and December 2016. Data was collected on pre-specified parameters including: basic demographics, histology, treatment response, completion rates, time from diagnosis to disease recurrence, site of disease recurrence, subsequent treatment and survival.

Results A total of 26 patients were identified. 65% of patents had adenocarcinoma and 35% squamous cell carcinoma. Of the 26 patients, 16 were receiving neoadjuvant chemoradiotherapy while 10 had definitive treatment, 3 of whom had local relapse and were having salvage definitive CRT. All bar 2 patients completed planned treatment; one due to oesophageal fistula formation and one due to poor tolerance - these were excluded from the analysis of disease recurrence. With a median follow-up of 15 months (range 7 - 31 months) for the patients who completed treatment, 92% remain alive and 17% (4/24) have recurred. Median time to disease recurrence was 11 months (range 10 - 14 months), 1 patient had isolated nodal recurrence and was treated with radical CRT, 3 had distal metastases.

Conclusion In this community-based cohort of patients with primary oesophageal or oesophagogastric-junction cancer, carboplatin/paclitaxel was feasible and well tolerated. With median follow-up of 15 months, 83% of patients remain disease free.

81

Efficacy and safety of liposomal irinotecan (nal-IRI) + 5-fluorouracil and leucovorin in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) who previously received gemcitabine-based therapy: post hoc analysis of the NAPOLI-1 trial

Floris A de Jong[1], Li-Tzong Chen[2], Andrea Wang-Gillam[3], Yan-Shen Shan[4], Teresa Macarulla[5], Jean-Frédéric Blanc[6], Richard A Hubner[7], Chang-Fang Chiu[8], Gilberto Schwartsmann[9], Jens T Siveke[10], Bruce Belanger[11], Khalid K Mamlouk[11], Daniel D Von Hoff[12]

1. Shire GmbH, Zug, Switzerland

2. National Health Research Institutes (NHRI) - National Institute of Cancer Research, Tainan, Taiwan
3. Washington University in St. Louis, St. Louis, MO, USA
4. Department of Surgery, National Cheng Kung University Hospital, Tainan, Taiwan
5. Vall d'Hebron University Hospital (HUVH) and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain
6. Pôle ADEN, Hôpital Haut-Lévêque, CHU Bordeaux, Bordeaux, France
7. Christie Hospital NHS Foundation Trust, Manchester, UK
8. China Medical University Hospital, Taichung, Taiwan
9. Federal University of Rio Grande do Sul, Porto Alegre, Brazil
10. West German Cancer Center, University Hospital Essen, Essen, Germany
11. Ipsen Bioscience, Inc., Cambridge, MA, USA
12. TGen and Honor Health, Phoenix/Scottsdale, AZ, USA

Background: nal-IRI+5-FU/LV is approved in Australia, the European Union, the United States and Taiwan for patients with mPDAC previously treated with gemcitabine-based therapy, based on the NAPOLI-1 study, which showed that nal-IRI+5-FU/LV improved OS vs 5-FU/LV (6.1 vs. 4.2 months; HR=0.67 [95% CI, 0.49–0.92]; *P*=0.012).[1] This *post hoc* analysis evaluated the efficacy and safety of nal-IRI+5-FU/LV in patient subgroups defined by prior gemcitabine regimen, including prior gemcitabine monotherapy and gemcitabine combinations.[2]

Methods: This analysis focuses on the 236 patients assigned to nal-IRI+5-FU/LV Q2W (n=117) or 5-FU/LV 4WQ6W (n=119). Patients previously received gemcitabine-based therapy in a neoadjuvant, adjuvant, locally advanced, or metastatic setting.

Results: Of patients in the nal-IRI+5-FU/LV arm (n=117), 53 (45%) previously received monotherapy and 64 previously received gemcitabine combinations, including erlotinib (n=9) or nab-paclitaxel (n=20). Of 119 patients in the 5-FU/LV arm, 55 (46%) previously received gemcitabine monotherapy and 64 previously received gemcitabine combinations, including erlotinib (n=17) or nab-paclitaxel (n=11). Compared with 5-FU/LV, nal-IRI+5-FU/LV improved median OS (gemcitabine monotherapy: 7.1 vs. 4.3 months; HR=0.81 [95% CI, 0.54–1.22]; *P*=0.31 and gemcitabine combinations: 6.1 vs. 4.2 months; HR=0.70 [95% CI, 0.48–1.02]; *P*=0.06), median PFS (gemcitabine monotherapy: 4.1 vs. 2.2 months; HR=0.63 [95% CI, 0.41–0.95]; *P*=0.03 and gemcitabine combinations: 3.1 vs. 1.4 months; HR=0.54 [95% CI, 0.36–0.81]; *P*<0.01), and ORR (gemcitabine monotherapy: 15% vs. 2%; *P*=0.02 and gemcitabine combinations: 19% vs. 0%; *P*<0.01), regardless of prior therapy. Grade ≥3 treatment-emergent adverse events were not influenced by prior treatment.

Conclusions: These results show a consistent benefit of nal-IRI+5-FU/LV treatment across subgroups of patients who previously received gemcitabine therapy and support ASCO guidelines recommending nal-IRI+5-FU/LV for this patient population. These analyses may be limited by the small sample size of treatment arms.

1. Wang-Gillam, A., et al. Lancet, 2016;387(10018):545–57.
2. This abstract was originally presented at ASCO-GI 2017: J Clin Oncol, 2017;35(suppl 4S): abstract 303.

82

Potential role of circulating tumor DNA (ctDNA) in the early diagnosis and post-operative management of localised pancreatic cancer.

Belinda Lee[1, 3, 2], Joshua Cohen[4], Lara Lipton[5, 2], Jeanne Tie[5, 1, 2], Lu Li[4], David Goldstein[6], Matthew Burge[7], Prasad Cooray[8], Adnan Nagrial[9], Niall Tebbutt[10], Mehrdad Nikfarjam[10], Marion Harris[11], Anne-Marie Lennon[4], Christopher L Wolfgang[4], Nikolas Papadopoulos[4], Cristian Tomasetti[4], Kenneth W Kinzler[4], Bert Vogelstein[4], Peter Gibbs[5, 1, 3, 2]

1. Walter & Eliza Hall Institute (WEHI), Melbourne, VIC, Australia
2. The Royal Melbourne Hospital, Parkville, Melbourne, VIC, Australia
3. Faculty of Medicine & Health Sciences, University of Melbourne, Melbourne, VIC, Australia
4. Johns Hopkins University, Baltimore, USA
5. Western Health, Melbourne, VIC, Australia
6. Prince of Wales Hospital, Sydney, NSW, Australia
7. Royal Brisbane Hospital, Brisbane, QLD, Australia
8. Eastern Health, Boxhill, Melbourne, Victoria, Australia
9. Crown Princess Mary Centre, Westmead, NSW, Australia
10. Austin Health, Melbourne, Victoria, Australia
11. Monash Cancer Centre, Melbourne, VIC, Australia

Background: Circulating tumour DNA (ctDNA) has shown promise as a screening test for various tumor types. The detection of ctDNA post curative intent surgery has been associated with a high risk of recurrence in multiple solid tumors. We explored the role of ctDNA in the pre and post-surgical setting to improve pancreatic cancer outcomes.

Methods: Data from separate US and Australian series were combined. Plasma samples were collected prior to surgery in both studies and post-operative from the Australian cohort from cases undergoing curative intent surgery. Clinicians were blinded to ctDNA results and adjuvant therapy was at clinician discretion. Tissue samples from both series were analyzed at Johns Hopkins University. Next generation sequencing was used to search for somatic KRAS mutations in the primary tumors and in cell-free DNA in the plasma. Clinico-pathologic, treatment and outcome data were collected.

Results: 119 pts had a ctDNA sample at diagnosis (median age 67 years, 56.3% male). Sixty six pts (55.5 %) had detectable ctDNA, including 3/7 (42.9%) with stage I disease, 54/99 (54.5%) with stage II disease, 4/8 (50%) with stage III disease and 5/5 (100%) with metastases. At preliminary analysis, specific codon 12 mutation (G12D, G12V or G12R) KRAS mutations were identified in the tumor tissue of 12/16 (75%) patients who had a ctDNA sample collected post-surgery. At a median follow-up of 15.2 months, 7/12 (58.3%) pts had recurred, including 3/8 (37.5%) with no detectable ctDNA and 4/4 (100%) with detectable ctDNA post-surgery (HR 4.9, p=0.04). Detectable ctDNA post-surgery was significantly associated with poor overall survival (HR 6.93, p = 0.006), with a median of 8 months for pts with detectable ctDNA. Further analysis is underway.

Conclusions: The detection of ctDNA post-operatively predicts a very high risk of recurrence. The clinical utility of ctDNA to guide adjuvant therapy decision making, and its potential as a real-time marker of treatment effect, are being explored in further studies.

83

Targeting Fibroblast Growth Factor Receptor (FGFR) with Regorafenib: preclinical and clinical data in oesophago-gastric cancer

Andrew Martin[1], David Williams[2], Fiona Chionh[3], Andrew Weickhardt[3], Katrin Sjoquist[4], Nick Pavlakis[5], John Mariadason[3], Niall Tebbutt[3], David Lau

1. NHMRC Clinical Trials Centre, Sydney

2. Austin Health, Heidelberg, VIC, Australia

3. Olivia Newton-John Cancer Research Institute, Heidelberg, VIC, Australia

4. St George Cancer Care Centre, Sydney, Sydney

5. Royal North Shore Hospital, Sydney

Introduction

Fibroblast growth factor receptor (FGFR1, 2, 3 and 4) overexpression is frequently observed in oesophago-gastric cancers and are associated with poor clinical outcomes[1]. Regorafenib inhibits the activity of multiple kinases, including FGFRs. We investigated the growth inhibitory effect of regorafenib on FGFR amplified or overexpressing gastric cancer cell lines in vitro and assessed clinical response to regorafenib in this subset of patients in the INTEGRATE trial.

Methods

Preclinical activity of regorafenib was evaluated in a panel of 25 gastric cancer cell lines. We conducted a post-hoc biomarker analysis of the phase II randomised, placebo controlled INTEGRATE clinical trial in advanced oesophago-gastric cancer. FGFR2 amplification was assessed by chromogenic in-situ hybridisation and FGFR1, 2 3 and 4 overexpression by multi-spectral immunohistochemistry.

Results

Treatment of four gastric cancer cell lines harbouring FGFR amplification and/or overexpression with regorafenib resulted in marked growth inhibition (GI_{50} range 0.1-1uM) suggesting FGFR expression as a biomarker of regorafenib activity. Tumour samples were available for 36 (24%) patients from the INTEGRATE trial. FGFR2 amplification was detected in 3 (8.3%) cases and all overexpressed FGFR2. FGFR1, 2, 3, 4 overexpression occurred in 13.9%, 19.4%, 16.6% and 13.9% of cases respectively. Patients overexpressing FGFR1, 2, 3 or 4 exhibited a significantly poorer progression free survival (HR: 2.99, 95% CI: 1.11 to 8.11, p-value = 0.02).

Conclusion

Gastric cancer cell lines with FGFR amplification or overexpression were exquisitely sensitive to regorafenib in vitro. However, no evidence of clinical activity was observed in patients with FGFR amplified or overexpressing tumours in the INTEGRATE clinical trial. Evaluation in a phase III cohort (INTEGRATE II) is planned.

1. Murase, H., et al., *Prognostic significance of the co-overexpression of fibroblast growth factor receptors 1, 2 and 4 in gastric cancer.* Molecular and Clinical Oncology, 2014. **2**(4): p. 509-517.

84

Institutional Variation in adherence to Quality of care indicators and their correlation with survival in patients with metastatic Colorectal cancer in Australia

Evangeline J Ponnusamy[1], Christine Semira [2], Margaret Lee[2, 3, 4, 5], Belinda Lee[2, 5], Jeremy Shapiro[6], Rachel Wong[2, 4], Louise Nott[7], Suzanne Kosmider[3], Ross Jennens [8], Desmond Yip[9, 10], Peter Gibbs[2, 3, 5]

1. Peter MacCallum Cancer Centre, Keysborough, VICTORIA, Australia

2. Walter and Eliza Hall Institute of Medical Research, Parkville, victoria, Australia

3. Medical Oncology, Western Health, Footscray, Victoria

4. Medical Oncology, Eastern Health, Box Hill, Victoria, Australia

5. The University of Melbourne, Parkville, Victoria, Australia

6. Medical Oncology, Cabrini Health, Malvern, Victoria, Australia

7. Royal Hobart Hospital, Hobart, Tasmania, Australia

8. Epworth Hospital, Richmond, Victoria, Australia

9. Canberra and Calvary Hospitals, Garran , canberra , Australia

10. ANU Medical School, Canberra, Canberra , ACT , Australia

Background:

Novel multidisciplinary quality of care indicators (QCIs) have been identified to set benchmarks in colorectal cancer care. we evaluated current variations in practice in relation to these putative QCIs across hospitals in Australia and their correlation with survival.

Methods:

Data related to demographics, performance status, and other previously identified 13 QCIs were extracted from the Treatment of Recurrent and Advanced Colorectal Cancer (TRACC) registry, a prospective database recording comprehensive details on metastatic colorectal cancer (mCRC) patients across Australian hospitals. This study was supported by Roche Products, Pty. Limited (Australia), by providing financial assistance for the development, installation and maintenance of this clinical database. Chi-square analysis was done to compare differences in QCIs. Log-rank tests and Cox regression analysis were used to correlate these QCIs with survival.

Results:

From July 2009 to June 2016, information on a total of 1602 patients across seven hospitals was analyzed. The cohorts differed significantly in terms of their age (>75 years) and ECOG status (p=0.037 and p=0.00 respectively). Comparative analyses suggested a wide variation in the quality of care of mCRC patients. Lung metastases resection rates (p=0.008), administration of first line palliative chemotherapy (p=0.00), rates of chemotherapy 30 days before death (p=0.004), clinical trial participation (p=0.00), palliative care referral rates (p=0.00) and recurrence screening methods (p=0.049) varied significantly among hospital sites. A significant difference between survival rates was noted amongst institutions (p=0.031). Liver and lung metastases resection rates (p=0.00 and p=0.046 respectively), administration of first line palliative chemotherapy (p=0.00), having palliative care referral (p=0.019) and treatment intent (p=0.00) all correlated with improved survival outcomes.

Conclusion:

There is significant variation in practice across hospitals in the proposed QCI. Here we demonstrate that some of this variation appears to impact survival outcomes. Further analysis is planned, in addition to routinely reporting back to sites a comparison of their QCI performance with other de-identified sites. This would allow sites an opportunity to review their performance and potentially identify areas for improvement.

85

Pharmacokinetics of anticancer drugs used in treatment of older patients with colorectal cancer: a systematic review.

Robert Yoon[1], Andrew McLachlen[2, 3], Alan Boddy[2], Philip Beale[4, 1], Prunella Blinman[4, 1], Mohsen Shafiei[4, 1]

1. Medical Oncology, The Concord Repatriation General Hospital, Concord, NSW, Australia

2. Pharmacology, The University of Sydney, Sydney, NSW, Australia

3. Pharmacy and aged care, The Concord Repatriation General Hospital, Concord, NSW, Australia

4. Medicine, The University of Sydney, Sydney, NSW, Australia

Background: Older adults with cancer experience greater toxicity from anticancer agents, but whether this is due to age-related changes in the pharmacokinetic (PK) profile of anticancer drugs is unclear. We sought to find, evaluate and summarise studies determining the effect of ageing on the PK of anticancer drugs commonly used in the treatment of colorectal cancer.

Methods: A literature search of the electronic databases EMBASE and PUBMED was conducted by two independent reviewers (MS, RY). Studies were included if they assessed the effect of age on the PK characteristics of chemotherapy or biologic anticancer drugs used in the treatment of colorectal cancer.

Results: The 21 included studies were either prospective studies or pooled PK data analyses of prospective studies. Of these, PKs of 5-FU (dose range 320–2400 mg/m^2) were determined in 7 studies, oxaliplatin (50 to 130mg/m^2) in 2 studies, capecitabine (1000 mg/m^2) in 3 studies, irinotecan (20 to 340 mg/m^2) in 4 studies, bevecizumab (5 mg/kg) in 1 study, cetuximab (250 mg/m^2) in 3 studies and panitumumab (0.01-9 mg/kg) in 1 pooled analysis of 14 prospective studies. While 6 studies determined the PK of the anticancer drugs in colorectal cancer, 15 articles concerned other cancer types. Studies included a median of 44 patients (range 19 to 1200) with the age definition of an older adult varying across studies (≥65, 70 or 75 years). PK parameters significantly affected by age were drug clearance, AUC, Cmax and Vmax (8 studies). Older age significantly affected PK parameters of irinotecan only [AUC (p=0.007) and Cmax (p= 0.009)].

Conclusion: Older age affected the PKs of irinotecan, but not other anticancer drugs used in the management of colorectal cancer. Factors other than PK may be responsible for the greater toxicity of these agents in older adults.

45

The potential of circulating tumor DNA (ctDNA) to guide adjuvant chemotherapy decision making in locally advanced rectal cancer (LARC)

Jeanne Tie, Margaret Lee, Joshua Cohen, Yuxuan Wang, Lu Li, Isaac Kinde, Hany Elsaleh, Rachel Wong, Suzanne Kosmider, Desmond Yip, Ben Tran, Matthew Burge, David Goldstein, Madhu Singh, Luis Diaz, Christian Tomasetti, Nickolas Papadopoulos, Kenneth Kinzler, Bert Vogelstein, Peter Gibbs

Background: The optimal approach to adjuvant chemotherapy for rectal cancer is keenly debated. Routine practice and clinical guidelines vary widely. After pre-operative chemoradiation (CRT), a pathologic complete response (pCR) or nodal involvement (pN+) are prognostic markers that can guide clinical decision-making, but markers that better define the patients that are likely or unlikely to benefit from chemotherapy are urgently needed. We investigated the potential role of ctDNA as a biomarker to guide therapy.

Methods: We conducted a prospective, multi-centre study in patients with LARC (T3/T4 and/or N+) planned for CRT and curative resection. Serial plasma samples were collected pre-CRT, post-CRT, and 4-10 weeks after surgery. Somatic mutations in individual patients' tumor were identified via sequencing of 15 genes commonly mutated in colorectal cancers. We then designed personalized assays to quantify ctDNA in plasma samples. Patients received adjuvant therapy at clinician discretion.

Results: 200 patients were enrolled between Apr-2012 and Dec-2015. Median age was 62 years (range 28-86) and 159 patients had pre-CRT and post-op ctDNA samples available for analysis. Of these, 122 (77%) patients had detectable ctDNA prior to therapy. After surgery, 19 patients had detectable ctDNA and 11 of these 19 (58%) have recurred during a median follow up of 24 months. Recurrence occurred in only 12 of 140 (8.6%) with negative ctDNA (HR 12, $p < 0.001$). 102 (64%) patients received adjuvant chemotherapy. Post-op ctDNA detection was predictive of recurrence irrespective of adjuvant chemotherapy (chemo: HR 9.2, $p < 0.001$; no chemo: HR 16, $p < 0.001$). Thirty-four patients (21%) achieved a pCR, 43 (27%) had pN+ disease. pCR (vs non-pCR) was associated with a trend for lower recurrence risk (HR 0.31, $p = 0.1$) and pN+ (vs pN0) with a higher recurrence risk (HR 4.3, $p < 0.001$). ctDNA detection remained predictive of recurrence among patients with a pCR (HR 15, $p = 0.01$) or with pN+ disease (HR 11, $p < 0.001$).

Conclusions: Post-op ctDNA analysis stratifies patients with LARC into very high and low risk groups. ctDNA analysis remains strongly predictive of recurrence among patients with both lower risk (pCR) and higher risk (pN+) disease.

86

Optimal care pathways in Gastro Intestinal Cancers

Christine Bishop[1]

1. AGITG Consumer Advisory Panel, Dawes Point, NSW, Australia

Optimal Care Pathways (OCPs) in cancer care have been endorsed for national implementation in Australia http://www.cancer.org.au/health-professionals/optimal-cancer-care-pathways.html.

Four (of the 15) OCPs are of interest to Gastrointestinal Cancer patients and clinicians:

Colorectal Cancer

Hepatocellular Carcinoma

Oesophagogastric Cancer and
Pancreatic Cancer

The individual OCPs are designed as care trajectories for clinicians, patients, their carers. We see two purposes:

1. To provide not only 'best practice' guidance for clinicians ('optimal treatment') at each stage of an individual's cancer journey but also
2. To promote understanding by the patient and their carers of the overall OCP and its distinct components and phases, aiming to ameliorate the entire experience of, in general, an overwhelmingly traumatic event.

Each individual OCP comprises two versions, a brief Summary detailing the steps of each OCP from Prevention and Early Detection to End of Life Care and then a longer section detailing the components of each Stage.

AGITG CAP members examined the four OCPs relevant to G I Cancers, from the patient's and carers' perspectives, to determine to what extent those OCPs fulfil the second purpose of improved patient understanding and experience for which they were established. We asked:

1. How easily will patients be able to comprehend and assimilate the information provided so OCPs satisfy patient as well as clinician needs?
2. While acknowledging individual OCPs vary to take into account differences in cancers, do they also consider sufficiently, the heterogeneity of cancer patients such as age, education, culture and socio-economic level? In concentrating on clinical aspects, do OCPs sufficiently consider psychosocial aspects of treatment?

Notwithstanding the obvious benefits of the OCPs, how can we ensure already financially stressed health budgets can afford to implement such broad based Multi Disciplinary Teams and supply the highly trained personnel required.?

87

Subgroup analysis by prior non-liposomal irinotecan therapy in NAPOLI-1: a phase 3 study of nal-IRI±5-fluorouracil/leucovorin in patients with metastatic pancreatic ductal adenocarcinoma previously treated with gemcitabine-based therapy

Andrew Dean[1], Jean-Frédéric Blanc[2], Richard A Hubner[3], Chung-Pin Li[4], Andrea Wang-Gillam[5], György Bodoky[6], Yan-Shen Shan[7], Teresa Macarulla[8], Kyung-Hun Lee[9], David Cunningham[10], Chang-Fang Chiu[11], Gilberto Schwartsmann[12], Fadi S Braiteh[13], Daniel D Von Hoff[14], Li-Tzong Chen[15], Khalid K Mamlouk[16], Floris A de Jong[17], Jens T Siveke[18]

1. St John of God Subiaco, Subiaco, WA, Australia

2. Pôle ADEN, Hôpital Haut-Lévêque, CHU Bordeaux, Bordeaux, France

3. Christie Hospital NHS Foundation Trust, Manchester, UK

4. Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

5. Washington University in St. Louis, St. Louis, MO, USA

6. Szent László Hospital, Budapest, Hungary

7. Department of Surgery, National Cheng Kung University Hospital, Tainan, Taiwan

8. Vall d'Hebron University Hospital (HUVH) and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

9. Department of Internal Medicine and Cancer Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

10. Royal Marsden NHS Foundation Trust, London and Surrey, UK

11. China Medical University Hospital, Taichung, Taiwan

12. Federal University of Rio Grande do Sul, Porto Alegre, Brazil

13. Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA

14. TGen and Honor Health, Phoenix/Scottsdale, AZ, USA

15. National Health Research Institutes (NHRI) – National Institute of Cancer Research, Tainan, Taiwan

16. Ipsen Bioscience, Inc., Cambridge, MA, USA

17. Shire GmbH, Zug, Switzerland

18. West German Cancer Center, University Hospital Essen, Essen, Germany

Background: In the global, randomized phase 3 NAPOLI-1 study, liposomal irinotecan (nal-IRI) + 5-fluorouracil/leucovorin (5-FU/LV) significantly increased median OS vs 5-FU/LV by 45% (6.1 vs. 4.2 months; unstratified hazard ratio (HR)=0.67 [95% CI, 0.49–0.92]; *P*=0.012) in patients with metastatic pancreatic ductal

adenocarcinoma who have progressed following gemcitabine-based therapy. Here, we present a subgroup analysis by prior non-liposomal irinotecan (NLI).[1]

Methods: Study methodology has been published.[2] Robustness of overall treatment effect was assessed by prospectively-defined subgroups, including prior NLI, based on primary survival analysis data (cut-off February 2014) of the ITT population.

Results: In patients with prior NLI, nal-IRI+5-FU/LV (n=12 [10%]) and 5-FU/LV (n=17 [14%]) treatment exhibited similar median OS (4.6 vs. 4.8 months; HR=1.25 [95% CI, 0.49–3.19], *P*=0.64), PFS (1.5 vs. 1.4 months; HR=0.83 [95% CI, 0.34–2.02], *P*=0.66) and CA19-9 response (0/10 vs. 0/10). In patients without prior NLI, nal-IRI+5-FU/LV (n=105) improved median OS (6.7 vs. 4.2 months; HR=0.62 [95% CI, 0.44–0.86]; *P*<0.01), median PFS (3.5 vs. 1.5 months; HR=0.52 [95% CI, 0.37–0.71]; *P*<0.0001) and CA19-9 response (28/87 [32%] vs. 7/71 [10%]; *P*<0.001) vs. 5-FU/LV (n=102). Most frequent TEAEs were gastrointestinal disorders (diarrhea, vomiting, nausea), regardless of prior NLI. ≥Grade 3 TEAEs and TEAEs leading to dose modification were similar in patients with (9 [75%]; 6 [50%]) and without (81 [77%]; 77 [73%]) prior NLI in the nal-IRI+5-FU/LV arm.

Conclusion: This post-hoc subgroup analysis shows significant increases for nal-IRI+5-FU/LV vs. 5-FU/LV in OS, PFS and CA19-9 response rates in patients without prior NLI. Outcomes were similar in both arms in patients with prior NLI. The low number of patients with prior NLI preclude firm conclusions from being drawn and further research is needed to explore the impact of prior NLI.

1. This abstract was originally presented at ESMO-GI 2017: Ann Oncol 2017;28(suppl_3): mdx263.017
2. Wang-Gillam, A., et al. Lancet, 2016;387(10018):545–57.

88

Subgroup analysis by prior lines of metastatic therapy (mtx) in NAPOLI-1, a global, randomized phase 3 study of liposomal irinotecan (nal-IRI) ± 5-fluorouracil and leucovorin (5-FU/LV), vs. 5-FU/LV in patients with metastatic pancreatic ductal adenocarcinoma who have progressed following gemcitabine-based therapy

Andrew Dean[1], Teresa Macarulla[2], Jens T Siveke[3], Andrea Wang-Gillam[4], Chung-Pin Li[5], György Bodoky[6], Yan-Shen Shan[7], Kyung-Hun Lee[8], Jean-Frédéric Blanc[9], Chang-Fang Chiu[10], Gilberto Schwartsmann[11], Fadi S Braiteh[12], David Cunningham[13], Li-Tzong Chen[14], Daniel D Von Hoff[15], Khalid K Mamlouk[16], Floris A de Jong[17], Richard A Hubner[18]

1. St John of God Subiaco, Subiaco, WA, Australia

2. Vall d'Hebron University Hospital (HUVH) and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

3. West German Cancer Center, University Hospital Essen, Essen, Germany

4. Washington University in St. Louis, St. Louis, MO, USA

5. Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

6. Szent László Hospital, Budapest, Hungary

7. Department of Surgery, National Cheng Kung University Hospital, Tainan, Taiwan

8. Department of Internal Medicine and Cancer Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

9. Pôle ADEN, Hôpital Haut-Lévêque, CHU Bordeaux, Bordeaux, France

10. China Medical University Hospital, Taichung, Taiwan

11. Federal University of Rio Grande do Sul, Porto Alegre, Brazil

12. Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA

13. Royal Marsden NHS Foundation Trust, London and Surrey, UK

14. National Health Research Institutes (NHRI) – National Institute of Cancer Research, Tainan, Taiwan

15. TGen and Honor Health, Phoenix/Scottsdale, AZ, USA

16. Ipsen Bioscience, Inc., Cambridge, MA, USA

17. Shire GmbH, Zug, Switzerland

18. Christie Hospital NHS Foundation Trust, Manchester, UK

Background:

In the NAPOLI-1 study, nal-IRI+5-FU/LV significantly increased median OS vs. 5-FU/LV control (6.1 vs. 4.2 months; unstratified HR=0.67 [95% CI, 0.49–0.92]; *P*=0.012). This is a subgroup analysis by prior lines of mtx.[1]

Methods:

Study methodology has been published.[2] This exploratory subgroup analysis compares outcomes in patients with 0–1 vs. ≥2 prior mtx lines, based on primary survival analysis data (cut-off February 2014) of the intent-to-treat population.

Results:

In the nal-IRI+5-FU/LV arm, 77 patients had 0–1 prior mtx lines (66%) and 40 patients had ≥2 prior mtx lines. In the 5-FU/LV arm, 82 (69%) patients had 0–1 prior mtx lines and 37 patients had ≥2 prior mtx lines. In patients with 0–1 prior lines of mtx, treatment with nal-IRI+5-FU/LV showed improvements vs. 5-FU/LV in OS (6.2 vs. 4.2 months; HR=0.66 [95% CI, 0.45–0.96]; *P*=0.03), progression free survival (PFS) (2.9 vs. 1.5 months; HR=0.51; [95% CI, 0.35–0.73]; *P*<0.001) and CA19-9 response rate (21/68 [31%] vs. 6/56 [11%]; *P*<0.01). In patients with ≥2 prior lines of mtx, treatment with nal-IRI+5-FU/LV also showed improvements vs. 5-FU/LV in OS (5.4 vs. 4.3 months; HR=0.68 [95% CI, 0.38–1.20]; *P*=0.18), PFS (4.0 vs. 1.6 months; HR=0.65 [95% CI, 0.37–1.14]; *P*=0.13) and CA19-9 response rate (7/29 [24%] vs. 1/25 [4%]; *P*=0.06). The safety profile was similar between subgroups receiving nal-IRI+5-FU/LV treatment (≥grade 3 drug-related AEs: 43 [55%] with 0–1 and 20 [51%] with ≥2 prior mtx lines).

Conclusions:

This post-hoc subgroup analysis shows significant increases for nal-IRI+5-FU/LV over 5-FU/LV in OS, PFS and CA19-9 response in patients with 0–1 prior mtx lines. Median OS benefit was less prominent in later lines, but conclusions are restricted by limited patient numbers.

1. This abstract was originally presented at ASCO 2017: J Clin Oncol, 2017;35(suppl 15): abstract 4127.
2. Wang-Gillam, A., et al. Lancet, 2016;387(10018):545–57.

89

Translational studies from the ASCOLT international trial: Feasibility of tissue collection and processing from AGITG sites

Eva Segelov[1], Shan Li[2], Marie Parsons[2], Sonia Yip[3, 4], Christine Aiken[3], David Williams[5], Michael Christie[6], John Chai Whay Kuang[7], Oliver Sieber[2]

1. Monash Health, Clayton, VIC, Australia

2. Walter and Eliza Hall Institute of Medical Research, Melbourne

3. NHMRC Clinical Trials Centre, University of Sydney, Sydney

4. Sydney Catalyst Translational Cancer Research Centre, University of Sydney, Sydney

5. Austin Pathology, Melbourne

6. Royal Melbourne Hospital, Melbourne

7. National Cancer Centre, Singapore

Background: In 2008, the International Aspirin for Dukes C and High Risk Dukes B Colorectal Cancers (ASCOLT) study was initiated as the first definitive Phase III trial of adjuvant aspirin v placebo in the secondary prevention of colorectal cancer. The Australasian Gastro-Intestinal Trials Group is leading the associated translational research, in particular examining biomarkers of aspirin benefit. We hypothesise that we can validate a signature of germline and tumour genomic and histopathologic markers to predict which patients will benefit from aspirin use, including the predictive value of *PIK3CA* mutations and PTGS2/COX-2 overexpression. The initial stage required collection of samples from patients enrolled in Australia and New Zealand.

Aim: To assess the consent rate and feasibility of collection of tissue samples from ASCOLT participants and to describe the process and quantify the usability of the specimens.

Methods: Data on consent and retrieval was obtained from a customised ASCOLT sample tracking database at NHMRC Clinical Trials Centre. Data on tissue sample handling was obtained from a master database at the central (Sieber) laboratory.

Results: 142 patient specimens (tissue blocks or slides) were collected from 188 patients consenting to donate tissue samples (84%) which represents samples from 63% of all recruited ASCOLT patients (224 patients as at June 2017) in two batches (2015/6: 81 samples and 2017: 61 samples, another 18 samples are pending retrieval). Slides were cut from blocks, stained with H&E and reviewed by a histopathologist (134 patients). 14 blocks were unusable (low% or NIL tumour cells). 5 slides each from 99 patients under went microdissection. DNA was extracted from 65 patients where the area of tumour epithelium exceeded 30%. To date, 49 patients had 5 slides stained with the following IHC markers: COX2, CD3, CD8, CD45RO, HLA Class I antigen. Stained slide images were digitally captured using Aperio software and are awaiting scoring by the histopathologist.

Conclusion: Translational research studies from large multicentre trials require considerable coordination for specimen collection and processing. Although considered extremely important as an adjunct to the clinical question, funding for translational research studies is not included in most primary trial budgets.

90

Trifluridine/tipiracil versus placebo plus best supportive care in patients with metastatic colorectal cancer refractory to standard therapies: Final survival results of the phase III RECOURSE trial.

Peter Gibbs[1], Ben Tran[2], Robert J Mayer[3], Atsushi Ohtsu[4], Takayuki Yoshino[5], Alfredo Falcone[6], Rocio Garcia-Carbonero[7], Josep Tabernero[8], Alberto F Sobrero[9], Marc Peeters[10], Fabio Benedetti[11], Lukas Makris[12], Hiroshi Ambe[13], Alberto Zaniboni[14], Yasuhiro Shimada[15], Kentaro Yamazaki[16], Yoshito Komatsu[17], Howard S Hochster[18], Heinz-Josef Lenz[19], Eric Van Cutsem[20]

1. Royal Melbourne Hospital, Parkville

2. The Royal Melbourne Hospital, Melbourne, VIC, Australia

3. Dana-Farber Cancer Institute, Boston, MA, USA

4. Exploratory Oncology Research & Clinical Trial Center, National Cancer Center, Kashiwa, Japan

5. National Cancer Center Hospital East, Kashiwa, Japan

6. Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy

7. Hospital Universitario Virgen del Rocio, Sevilla, Spain

8. Vall d'Hebron University Hospital, Barcelona, Spain

9. IRCCS A.O.U. San Martino IST, Genoa, Italy

10. Antwerp University Hospital, Edegem, Belgium

11. Taiho Oncology, Inc., Princeton, NJ, USA

12. Stathmi, Inc., New Hope, PA, USA

13. Taiho Pharmaceutical Co., LTD., Tokyo, Japan

14. Fondazione Poliambulanza, Brescia, Italy

15. National Cancer Center Hospital, Chuo-Ku, Japan

16. Shizuoka Cancer Center, Shizuoka, Japan

17. Hokkaido University Hospital, Sapporo, Japan

18. Yale Cancer Center, New Haven, CT, USA

19. USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA

20. University Hospitals Leuven, Leuven, Belgium

Background: Trifluridine/tipiracil (also known as TAS-102) is comprised of an antineoplastic thymidine-based nucleoside analog, trifluridine, and a thymidine phosphorylase inhibitor, tipiracil hydrochloride. Efficacy and safety of trifluridine/tipiracil in patients with metastatic colorectal cancer refractory/intolerant to standard therapies were evaluated in the RECOURSE trial. Original results of RECOURSE based on the cut-off date of January 24, 2014, in which 72% of mortality events had occurred, demonstrated a significant improvement in overall survival (OS) with trifluridine/tipiracil vs placebo. Here we report results of an updated survival analysis from RECOURSE and a retrospective analysis of OS outcomes based on a clinical prognostic risk index.

Methods: Patients were randomized 2:1 to receive trifluridine/tipiracil or placebo. Study treatment continued until disease progression, death, or unacceptable toxicity. The primary endpoint was OS; final survival data were collected on October 8, 2014. A clinical OS prognostic risk score was assessed to evaluate OS effect in patients from low to high prognostic score. Prognostic factors contributing to the risk index were from those prespecified in the multivariate modeling assessment of OS outcome.

Results: At data cut-off for the final survival analysis, 89% of the 800 patients randomly assigned to trifluridine/tipiracil or placebo had died, accounting for 138 events in addition to 574 (72%) events included in the original analysis. For the final analysis, median overall survival improved from 5.2 months with placebo to 7.2 months with trifluridine/tipiracil (HR, 0.69; 95% CI, 0.59-0.81; P<0.0001). 1-year survival improved from 16.6% (95% CI, 12.3-21.4) with placebo to 27.1% (95% CI, 23.3-30.9) with trifluridine/tipiracil.

Conclusions: An updated survival analysis confirmed that OS benefit with trifluridine/tipiracil was maintained and increased to a full 2 months; improvement in 1-year survival surpassed 10% in these heavily pretreated patients. OS benefit appears to be maintained for all patients in the trial regardless of prognostic status at trial entry

Clinical trial information: NCT01607957

47

Exploring Consensus Molecular Subtypes (CMS) as predictors of benefit from bevacizumab in first line treatment of metastatic colorectal cancer: retrospective analysis of the MAX clinical trial

Jennifer Mooi[1], Pratyaksha Wirapati[2], Rebecca Asher[3], Chee Khoon Lee[3], Peter Savas[4], Timothy J Price[5], Sabine Tejpar[6], John Mariadason[1], Niall C Tebbutt[7]

1. Olivia-Newton John Cancer Research Institute, Heidelberg, VIC, Australia

2. Bioinformatics Core Facility,, Swiss Institute of Bioinformatics, Lausanne, Switzerland

3. NHMRC Clinical Trials Centre, , University of Sydney, , Sydney,, NSW, Australia

4. Medical Oncology, , Peter MacCallum Cancer Center, , Melbourne, , VIC,, Australia

5. Medical Oncology, Queen Elizabeth Hospital and University of Adelaide, Woodville, SA, Australia

6. Oncology, University Hospital Leuven, Leuven, Belgium

7. Medical Oncology, Olivia Newton-John Cancer Centre and Austin Health, Heidelberg, VIC, Australia

Background: CMS is a transcriptome-based classification of colorectal cancer (CRC) with prognostic implications, but its association with treatment outcomes, especially in the metastatic setting, remains unknown. We investigated whether CMS classification was predictive of bevacizumab treatment benefit using data from the phase 3 MAX trial. MAX previously reported progression-free survival (PFS) benefit for the addition of bevacizumab (B) to chemotherapy (capecitabine (C) +/- mitomycin (M)) in first line treatment of metastatic CRC.

Methods: Archival tumours from 256 patients (54% of trial population) were available for gene expression profiling using Almac Xcel microarray. Tumours were classified into CMS groups 1 to 4 using previously published methods. We correlated CMS groups with PFS in the MAX trial. The predictive value of CMS was demonstrated as the interaction between CMS and bevacizumab treatment, assessed by Cox proportional hazards model.

Results: After data quality control, primary tumours from 239 patients (51% of trial population) were suitable for survival analysis. Distribution of CMS groups were CMS1 18%, CMS2 48%, CMS3 12%, CMS4 23%. Hazard ratios (HR)(95% CI) of PFS in C vs CB+CBM arms for CMS 1,2,3 and 4 were 0.83 (0.43-1.62), 0.50 (0.33-0.76), 0.31 (0.13-0.75) and 1.24 (0.68-2.25) respectively (test for interaction between CMS and treatment, p=0.03). CMS remained a significant independent predictor of PFS after adjustment for prognostic factors in a multivariate analysis (p=0.04).

Conclusions: In metastatic CRC, CMS 2 and 3 subtypes preferentially benefit from the addition of bevacizumab to chemotherapy, compared to CMS 1 and 4. Validation of these findings in independent cohorts is required. Once validated, CMS classification could be used to guide patient selection for bevacizumab therapy.

91

Onset of neutropenia as an indicator of treatment response in the phase 3 RECOURSE trial of trifluridine/tipiracil versus placebo in patients with metastatic colorectal cancer.

Nick Pavlakis[1], Atsushi Ohtsu[2], Takayuki Yoshino[3], Alfredo Falcone[4], Rocio Garcia-Carbonero[5], Guillem Argiles[6], Alberto F Sobrero[7], Marc Peeters[8], Lukas Makris[9], Fabio M Benedetti[10], Alberto Zaniboni[11], Yasuhiro Shimada[12], Kentaro Yamazaki[13], Yoshito Komatsu[14], Howard S Hochster[15], Heinz-Josef Lenz[16], Ben Tran[17], Kenichiro Yoshida[18], Eric Van Cutsem[19], Robert J Mayer[20]

1. Department of Medical Oncology , Royal North Shore Hospital, Sydney, NSW, Australia

2. National Cancer Center Hospital East, Kashiwa, Japan

3. National Cancer Center Hospital East, Chiba, Japan

4. Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy

5. Hospital Universitario Doce de Octubre, Madrid, Spain

6. Vall d' Hebron University Hospital and Institute of Oncology (VHIO), Universitat Autonoma de Barcelona, Barcelona, Spain

7. IRCCS A.O.U. San Martino IST, Genoa, Italy

8. Antwerp University Hospital, Edegem, Belgium

9. Stathmi, Inc., New Hope, PA, USA

10. Taiho Pharmaceutical Co., LTD., Tokyo, Japan

11. Fondazione Poliambulanza, Brescia, Italy

12. National Cancer Center Hospital, Chuo-Ku, Japan

13. Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan

14. Department of Cancer Chemotherapy, Hokkaido University Hospital Cancer Center, Sapporo, Japan

15. Yale Cancer Center, New Haven, CT, USA

16. USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA

17. The Royal Melbourne Hospital, Melbourne, VIC, Australia

18. Taiho Oncology, Inc., Princeton, NJ, USA

19. University Hospitals Leuven, Leuven, Belgium

20. Dana-Farber Cancer Institute, Boston, MA, USA

Background: Trifluridine/tipiracil (also known as TAS-102) is comprised of an antineoplastic thymidine-based nucleoside analog, trifluridine, and a thymidine phosphorylase inhibitor, tipiracil. Primary results of the RECOURSE trial demonstrated a significant improvement in overall survival and progression-free survival with trifluridine/tipiracil vs placebo in patients with metastatic colorectal cancer refractory/intolerant to standard therapies. Neutropenia is a common trifluridine/tipiracil–associated adverse event and it has been hypothesized to be associated with a relatively high trifluridine concentration in patients.

Methods: RECOURSE data were analysed post hoc for correlations between onset of neutropenia (Grade 3/4) and survival benefit.

Results: Of 533 patients given trifluridine/tipiracil, 75 (14%) developed Grade 3/4 neutropenia in treatment cycle 1, 86 (16%) for the first time in cycle 2, and 39 (7%) for the first time in cycle ≥3. The median time to nadir in cycle 1 for grade ≥3 neutropenia was 28 days (17–31). Onset of neutropenia at any cycle was associated with longer median OS and PFS compared with no neutropenia. A consistent survival benefit was observed for patients with neutropenia at cycle 1 (4.4 months 0.45(0.32-0.64) cycle 2 (2.4 months 0.56 (0.41-0.78) and cycle ≥3 (6.2 months 0.36(0.17-0.75) regardless of the cycle of initial onset of neutropenia, as demonstrated by the hazard ratio (against cycle-matched placebo control groups) and corresponding median OS differences.

Conclusions: An association between occurrence of earliest onset of Grade 3/4 neutropenia and survival benefit was observed. The data indicate that such survival benefit occurred regardless of whether the initial onset of neutropenia occurred after cycle 1, cycle 2, or later. Further analyses are required to fully determine whether trifluridine pharmacokinetics correlate with trifluridine/tipiracil efficacy and onset of neutropenia, and whether cycle initiation delays affect response.

Clinical trial information: NCT01607957

53

An audit of the long term outcomes of Western Australian patients undergoing peritonectomy

David Ransom[1], Angela Ives[2], Dhanvee Kandadai[3]

1. WA Cancer and Palliative Care Network, Department of Health. Government of Western Australia, Perth, WA, Australia

2. Cancer and Palliative Care Research and Evaluation Unit, , Medical School. The University of Western Australia, Perth, WA, Australia

3. CMOs Office, Government of Western Australia, Department of Health, Perth, WA, Australia

Background: Between 2008 and 2013 WA patients travelled to NSW to undergo peritonectomy. This audit will review the long term outcomes for these patients.

Methods: A retrospective audit of 63 WA patients thought to have undergone peritonectomy in NSW. Data collected included: demographics, pathology at primary cancer diagnosis in WA, subsequent hospitalisation in WA (number of admissions, reason and duration), subsequent use of chemotherapy and survival (time from peritonectomy to death or census date).

Results: Data was available on 42 patients who underwent peritonectomy; 20 (47.6%) male and 22 (52.4%) female. Median age at peritonectomy was 54.7 years (range 20.5, 77.5). Thirty two (76.2%) were alive at censor date. Median follow up was 3.5 years (range 0.2, 4.9). Type of primary cancer at diagnosis: colorectal (n = 12; 27%), appendiceal (n = 18; 43%) and other cancer including mesothelioma (n = 12; 30%). Median survival was 3.5 years (range 0.2, 7.6) and eight patients (19%) had redo peritonectomy. Median survival for patients diagnosed with colorectal (1.3 years; range 0.2, 4.9) was inferior compared to the rest of the group (3.7years; range 0.3, 7.6) (log rank - $X^2$8.5, df 1, p = 0.004). While the number of patients with mesothelioma was low they were all alive more than five years post peritonectomy.

Post peritonectomy the median number of hospital admissions was 14 (range 0, 70); the median duration of hospital admissions was one day (range 1, 113). The median number of WA hospital admissions and emergency(ER) attendances post peritonectomy was 20 (range 0, 29) when chemotherapy and routine follow up appointments were excluded. The most common symptoms at presentation were abdominal pain and nausea/vomiting.

Conclusions:

- Post peritonectomy patients have frequent admissions and ER attendances .
- Patients with colorectal cancer had the poorest survival.
- Patients with mesothelioma did surprisingly well.

92

Stage based variation in the impact of primary tumour side on early stage colorectal cancer recurrence and survival

Margaret Lee, Andrew MacKinlay, Christine Semira, Antonio Yepes, Belinda Lee, Chathurika K Hettiarachchige, Natalie Gunn, Jeanne Tie, Rachel Wong, Hui-li Wong, Iain Skinner, Ian Jones, James Keck, Suzanne Kosmider, Ben Tran, Kathryn Field, Peter Gibbs

Background

Multiple studies have defined the prognostic and potential predictive significance of primary tumour side in patients with metastatic colorectal cancer (CRC). Currently available data regarding the impact of primary tumour side in early stage disease is limited and inconsistent.

Methods

We explored clinical, pathologic, treatment and outcome data from a multi-site Australian CRC registry of consecutive cases diagnosed from 2003-2016. Tumours distal to the splenic flexure were considered a left primary (LP). The healthcare group at IBM Research Australia provided data analysis.

Results

For the 6551 patients identified, the median age at diagnosis was 69 years, 55.1% were male and the majority (62.8%) had a LP. Comparing survival outcomes according to right primary (RP) versus LP, time-to-recurrence (TTR) was similar in stage I (HR 0.68, 95% CI 0.35-1.33) and stage III (HR 1.14, 0.93-1.39), but longer in stage II RP patients (HR 0.68, 95% CI 0.52-0.90, p<0.01). Adjuvant chemotherapy provided consistent benefit in stage III disease regardless of tumour side. Overall survival (OS) was similar in stage I and II disease when comparing LP to RP patients, however in stage III RP disease, poorer OS (HR 1.25, 95% CI 1.01-1.54, p<0.05) and cancer-specific survival (CSS) (HR 1.49, 95% CI 1.14-1.93, p<0.01) was observed. Stage IV RP patients had poorer OS whether synchronous (HR 1.21, 95% CI 1.02-1.43, p<0.05) or metachronous (HR 1.32, 95% CI 1.08-1.60, p<0.01) in presentation.

Conclusions

In early stage CRC, the association of tumour side and impact upon TTR and OS varies by stage. In stage II RP disease, the improved TTR did not translate to a long-term survival benefit. In stage III patients with a RP, the poorer CSS is in part due to an inferior post-recurrence survival, rather than lack of benefit from adjuvant chemotherapy.

93

Is skeletal muscle a predictor of toxicity in pancreatic cancer patients on combination gemcitabine and nab paclitaxel chemotherapy?

Julia Freckelton[1], Daniel Croagh[1, 2], Darcy Holt[3], Adrian Fox[1, 4], Rachel Wong[1, 5], Margaret Lee[1, 5], Gregory T Moore[1, 6]

1. School of Clinical Sciences, Monash University, Clayton, VIC, Australia

2. Department of Surgery, Monash Health, Clayton, Vic, Australia

3. Clinical Nutrition and Metabolism Unit, Monash Health, Clayton, Vic, Australia

4. Department of Surgery, Eastern Health, Box Hill, Vic, Australia

5. Department of Medical Oncology, Eastern Health, Box Hill, Vic, Australia

6. Department of Gastroenterology and Hepatology, Monash Health, Clayton, Vic, Australia

Introduction

Combination gemcitabine and nab-paclitaxel (Gem-Nab-P) is a common regimen used to treat metastatic pancreatic ductal adenocarcinoma (PDAC). Toxicity is less than that associated with other combination metastatic regimens (FOLFIRINOX), but it is still associated with significant morbidity. Currently, Gem-Nab-P is dosed using estimated body surface area. This study investigates whether skeletal muscle assessment could be a useful tool in the dosing of Gem-Nab-P in metastatic PDAC.

Methods

This study involved two sites and included patients who had received treatment with Gem-Nab-P between January 2013 and March 2017. A review of medical records was used to identify demographic, disease and first-cycle treatment information. Chemotherapy toxicity was defined as grade 3 or 4 adverse events using the National Cancer Institute Common Toxicity Criteria Adverse Events manual v4.0. Body composition analysis was performed on computed tomography scans at anterior spinal level L3, using SliceOmatic software. SPSS software was used to assess significance of associations between chemotherapy toxicity and muscle attenuation, skeletal muscle area (SkMA) and dose to SkMA for all statistical analysis, with a p-value of <0.05 considered significant.

Results

We identified 52 patients treated with first-line Gem-Nab-P for PDAC. Median age was 65 years (57-73) and 24 (47%) were male. Median BMI at commencement of Gem-Nab-P was 24.7 kg/m^2 (21.3-27.4) and 38 (58%) of the patients were myopenic before starting chemotherapy. Fourteen (27%) patients experienced toxicity during the first cycle of chemotherapy.

Patients who experienced first-cycle chemotherapy-associated toxicity did not have a different median SkMA to those who did not (128.6 cm^2 v 111.4 cm^2, p= 0.2). There was also no difference in the gemcitabine dose to SkMA ratio (14.1 mg/cm^2 v 14.4 mg/cm^2, p=0.8), nab-paclitaxel to SkMA ratio (1.8 mg/cm^2 v 1.8 mg/cm^2, p=0.6) or combined dose equivalent to SkMA ratio (2.8 mg/cm^2 v 2.9 mg/cm^2, p=0.9) between the patients that experienced first cycle toxicity versus those that did not.

Conclusion

This study suggests that a pancreatic cancer patient's skeletal muscle area is unlikely to be a useful addition to conventional body surface area in the dosing of first line Gem-Nab-P, to reduce first-cycle toxicity.

52

Outcomes comparing right and left-sided metastatic colorectal cancer: A multi-centre retrospective analysis in Queensland, Australia

Michael J Allen[1, 2], Sophie Conroy[1], Melissa Eastgate[1, 2], David Wyld[1, 2], Vicki Whitehall[3], Matthew Burge[1, 2]

1. Department of Medical Oncology, Royal Brisbane and Women's Hospital, Herston, Queensland, Australia

2. School of Medicine, The University of Queensland, Brisbane, Queensland, Australia

3. QIMR Berghofer, Brisbane, Queensland, Australia

Background: Substantial biological heterogeneity is reported in metastatic colorectal cancer (mCRC) dependent on the side of the primary tumour, impacting on prognosis and potentially management decisions. We investigated these differences at three hospitals in Queensland.

Methods: A comprehensive database has been established of patients with mCRC across the Royal Brisbane & Women's Hospital, The Prince Charles Hospital and Rockhampton Base Hospital. Data was extracted on demographics, clinicopathologic features and outcomes compared by right (RS) and left-sided (LS) primary tumours. LS was defined as tumours distal to the splenic flexure.

Results: 153 patients were analysed, of which 115 (75%) were LS and 38 RS. There was no statistical difference in respect to tumour side for gender, mean age, BMI and ECOG status. The frequency of KRAS mutations was 37.5 v 42.3% (*p0.206*); BRAF mutations 25 v 5.8% (*p0.012*) and MSI 43.8 v 2.5% (*p<0.005*) for RS and LS respectively. Similar frequencies of treatment with chemotherapy (82 v 82%, *p1.000*) and first-line VEGF (53 v 45%, *p0.398*) or EGFR antibodies (2.6 v 8.8%, *p0.206*) was observed.

The incidence of synchronous metastases was 58 v 56% and metachronous 42 v 44% (*p0.809*). There were more lung metastases (13.2 v 33.9%, *p0.014*) and liver metastases (31.6 v 65.2%, *p<0.005*) in LS tumours. The rate of resection for RS and LS tumours was 23.7 and 37.4% (*p0.122*).

Overall survival (OS) was numerically higher in LS tumours (24.13 v 38.11m, *p0.111*) whilst progression free survival (PFS) was significantly higher (9.67 v 13.94m, *p0.005*), independent of KRAS status and treatment with VEGF or EGFR antibodies. BRAF and MSI median OS and PFS was not achieved and their implication on outcomes not analysed. Metastasectomy improved OS (RS 19.2-45.97m; LS 31.53-76.87m, *p<0.005*) and PFS (RS 8.47-11.39m; LS 10.93-24.28m, *p0.005*). This survival benefit was independent of location.

Conclusion: RS and LS tumours exhibit a different pattern of metastatic spread. RS tumours have a poorer prognosis despite similar systemic treatment and rates of resection. OS and PFS is markedly improved with the resection of metastases in both RS and LS malignancy suggesting metastasectomy, where possible, should be pursued for both primary sites.

94

Hepatic Resection for Colorectal Cancer with Liver Metastases: An Analysis Across Health Centres and Age Groups in Australia

Seema Kumari[1], Christine Semira[2], Margaret Lee[2, 3, 4, 5], Belinda Lee[2, 5], Rachel Wong[2, 4], Louise Nott[6], Jeremy Shapiro[7], Suzanne Kosmider[3], Desmond Yip[9, 8], Simone Steel[10], Sumitra Ananda[3], Lionel Lim[4], Babak Tamjid[11, 12], Matthew Burge[13], Peter Gibbs[2, 3, 5]

1. Victorian Comprehensive Cancer Centre, Parkville, VIC, Australia

2. Walter and Eliza Hall Institute of Medical Research, Parkville, VIC, Australia

3. Medical Oncology, Western Health, Footscray, VIC, Australia

4. Medical Oncology, Eastern Health, Box Hill, VIC, Australia

5. The University of Melbourne, Parkville, VIC, Australia

6. Royal Hobart Hospital, Hobart, TAS, Australia

7. Cabrini Health, Malvern, VIC, Australia

8. Canberra and Calvary Hospitals, Garran, ACT, Australia

9. ANU Medical School, Canberra, ACT, Australia

10. Peninsula Private Hospital, Frankston, VIC, Australia

11. Goulburn Valley Health, Shepparton, VIC, Australia

12. Rural Health Academic Centre, University of Melbourne, Shepparton, VIC, Australia

13. Royal Brisbane Hospital, Brisbane, QLD, Australia

Background: Colorectal cancer remains a common cancer in the western world, with liver resection being the only potentially curative option for isolated colorectal cancer liver metastases (CRCLM). This study aims to analyse the trend of hepatic resection for CRCLM across various hospitals in Australia, along with the frequency and outcome of resection among elderly patients.

Methods: We retrospectively collected and analysed patient data from 2009-2016 in the TRACC (Treatment of Recurrent and Advanced Colorectal Cancer) database (this study was supported by Roche Products, Pty. Limited, Australia, by providing financial assistance for the development, installation and maintenance of this clinical database). Information regarding resection rates and survival outcomes were obtained. Kaplan-Meier survival analysis was performed comparing overall survival (OS) and progression-free survival (PFS) between patients who had hepatic resection with those who did not.

Results: 775 patients with isolated CRCLM from 13 different hospitals were included, out of which 263 underwent hepatic resection. Rate of resection across hospitals was 30-32%. There was no statistically significant difference in the PFS and OS (p=0.27 & p=0.39 respectively) of patients who underwent hepatic resection among the different hospitals. In the elderly cohort (> 70 years old), there was a PFS and OS advantage (mean PFS 35.5 months versus 12.0 months, p<0.001; mean OS 56.2 months versus 18.1 months, p<0.001) for those who had liver resection. Similarly, in the very elderly (>80 years old), those who underwent resection had a significantly better PFS (mean PFS 31.2 months versus 11.1 months, p<0.001) and OS (mean OS 43.2 months versus 14.9 months, p<0.001) compared to those who did not have resection.

Conclusion: The frequency of hepatic resection for CRCLM and survival outcomes achieved across hospitals in Australia appears very similar. Liver resection in the elderly population selected for surgery appears to be associated with substantial survival gains.

95

Gastro-intestinal bleeding from metastatic disease - lobular breast cancer has a predilection for metastases to the GI tract.

Emily Clarke[1], Aesha Gandhi[1], James George[1], Stuart Paterson[1], Simon Weight[1], Corrine Jones[1], Andrew Dean[1]

1. St John of God Subiaco Hospital, Subiaco, WA, Australia

Background: Metastatic disease to the gastrointestinal tract is rare, with the possible exception of malignant melanoma. We add to our previously reported series of patients with metastatic breast cancer as an unusual source of gastrointestinal bleeding. Methods: An electronic database search was carried out using the search terms metastases, metastasis, GI bleeding, melena, oesophagus, stomach, small bowel and colon. The records of patients with proven metastases to the gastrointestinal tract identified in this way were then examined for demographic, pathologic and endoscopic data collection. Patients with malignant melanoma were excluded from analysis. Results: 5 patients were identified with proven non melanoma metastases to the GI tract, all were metastatic lobular breast cancer. The database contained 323 patients with breast cancer; 75 with infiltrating lobular breast carcinoma, 3 with micropapillary and 244 invasive ductal carcinoma. The first case presented with symptomatic anaemia. Colonoscopy revealed a polyp. Once removed, histopathology showed metastatic lobular breast carcinoma. Further investigation confirmed an occult breast mass with identical pathology. The 2nd case presented with 18 months of abdominal pain. After the onset of anaemia and 25kg weight loss, upper GI endoscopy

showed markedly thickened stomach. Biopsies confirmed metastatic lobular breast carcinoma. The third case presented with abdominal pain and raised CA125. Surgical debulking of ovarian and omental masses showed metastatic lobular breast carcinoma although no primary breast lesion was found at that stage. 3 years later, a colonoscopy for anaemia showed a caecal polyp with lobular breast carcinoma histology. The 4th case had confirmed metastatic lobular breast carcinoma on stomach biopsy which appeared thickened on gastroscopy for investigation of epigastric pain and nausea. The 5th case undergoing colonoscopy for investigation of nausea and abdominal distention with deranged LFTs and raised INR had 2 polyps confirming metastatic lobular breast carcinoma. Conclusion: After excluding melanoma, all 5 remaining cases with proven metastasis to the GI tract were cases of lobular breast cancer, even though all common tumour types were represented in the database. Further studies are needed to understand the mechanism behind the observation that lobular breast cancer has a predilection for metastasis to the GI tract compared to other common tumours.

96

Pneumocystis infection during first-line chemotherapy for solid tumours: Increased virulence or better diagnosis?

Talia James[1], Alex James[1], Marcela Nascimneto[1], Madeline Seeley[1], Dominic Higgs[1], AndrewAndrew Dean[1]

1. St john of God Subiaco, perth WA, Subiaco, WA, Australia

Background: Pneumocystis Jirovecii (PJP, previously Pneumocystis Carinii) infection is typically seen in those with advanced immunodeficiency such as Acquired Immunodeficiency Syndrome, haematological malignancies, sustained chemotherapy with temozolomide or patients heavily pretreated with multiple lines of chemotherapy. PJP rarely presents early in the natural history of solid tumour malignancy. We observed a cluster of cases of PJP at our institution in patients undergoing first-line chemotherapy for solid tumours.

Methods: An electronic database search was conducted to identify occurrences of PJP over a 3 month period. 4 patients were identified who developed Pneumocystis Jirovecii. The patients' records, laboratory, radiology and pathology results were examined.

Results: All 4 patients identified had developed PJP during first line chemotherapy for GI malignancy. In each case, the patient presented with dyspnoea, fever and hypoxia. All were noted to be lymphopenic with lymphocyte counts of 0.2 to 0.9 x10^9/L. All were HIV negative. Chest CT revealed new bilateral ground-glass changes associated with cyst formation. All cases were found to have positive PJP PCR on testing of induced sputum. On the basis of clinical presentation, positive PCR sputum cultures and CT findings, the patients were diagnosed with PJP and treated with highdose sulphamethoxazole and trimethoprim. 3 patients recovered and 1 died despite best ICU management.

Conclusions: The relatively high number of cases of PJP early in treatment is noteworthy. It raises the question as to whether PJP is becoming more potent or that better awareness leads to earlier and more accurate diagnosis. Coincidental clustering is also a possibility. Clinicians should be aware that pneumocystis infection can occur during first-line therapy in solid tumour malignancy. It should be considered as a differential in any patient on chemotherapy (regardless of line of therapy) presenting with acute respiratory illness.

97

Using mobile health applications (mHealth apps) to improve clinical trials: A consumer perspective.

Robin Mitchell[1], Grant Baker[1], Jan Mumford[1], Julie Marker[1], Autumn Tansey[1], Christine Bishop[1], Jeff Cuff[1], James Armstrong[1], Gillian Worden[1]

1. Consumer Advisory Panel, AGITG Consumer Advisory Panel, Camperdown , NSW, Australia

Using mobile health applications (mHealth apps) to improve clinical trials:
A consumer perspective.

Introduction:

There has been an explosion of mobile health applications (apps) over the last 10 years. The rapid emergence of apps for cancer care, allows consumers to manage their own care and may offer opportunities for clinicians and trial co-ordinators to engage with consumers. These apps not only offer enormous potential to involve and inform consumers, they could also provide a rich source of real time data to be utilised by cancer researchers.

The Australasian Gastro-Intestinal Trials Group (AGITG), Consumer Advisory Panel (CAP) set out to investigate the apps that are available to Australian cancer consumers. The purpose was to consider the benefits to patient care and potential for improving clinical trials.

Method:

The CAP members discussed several cancer related apps and the issues important to consumers. Where possible, developers were contacted to ascertain what the aim of their app was. The CAP then discussed the strengths and weaknesses of each app. A conclusion was reached on the usefulness apps could play in future cancer clinical trials.

Results:

A selection of mobile health apps for cancer care and clinical trials were assessed using a Strength, Weakness, Opportunities and Threat approach.

Strengths: Real time data collection.

Weaknesses: Inequity of technology access.

Opportunities: Improved clinical trial recruitment and participant engagement.

Threats: Privacy issues, governance and cost.

Conclusion:

Some apps researched were found to lack engagement with the consumer, under-utilised available technology and lacked the ability to consolidate the rich data collected.

It was concluded that the potential for apps in clinical trials is feasible, however concerns remained about level of consumer engagement, privacy, data ownership and access of the data.

Further work is needed on the apps to better engage with consumers, to fully utilise current technology and exploit available technology to consolidate data.

1. Kempf E, P. R.-M. (2016). Are Cancer Patients ready for e-medicine? Retrieved from: Bull Cancer 2016 Oct:103(10):841-848 doi 10.1016/j.bulcan,201606004Epub 2016 Aug.
2. Vries, G. d. (2016, April 5). Why Every Clinical Trial Should have an app for participants. Retrieved from www.statnews.com: https://www.statnes.com/2016/04/05/clinical-trial-drug-companies

98

The NETwork! Registry: Preliminary data suggests increasing incidence in a national study of neuroendocrine cancer in New Zealand (NZ)

Kate Parker[1], Esther Coats[1], Braden Woodhouse[1], Nicholas Knowlton, Ole Schmiedel[2], Richard Carroll[3], Marianne Elston[4], Dean Harris[5], Christopher Jackson[6], Jonathan Koea[7], Nicole Kramer[2], Mee-Ling Yeong[2], Masato Yozu[8], Reena Ramsaroop[7], Jeremy Rossaak[9], Helen Winter, Vince Newton[10], Alana Gould[3], Glenys Mahoney[11], Carol Jarvis[12], Debbie Skinner[13], Liz Thompson[5], Jodie Collinson[10], Melissa Firth[1], Jerome Macapagal[1], Cristin Print[1], Michael Findlay[1], Ben Lawrence[1]

1. University of Auckland, Grafton, AUCKLAND, New Zealand

2. Auckland District Health Board, Auckland

3. Wellington Hospital, Wellington

4. Waikato Clinical Campus, University of Auckland, Hamilton

5. Canterbury District Health Board, Christchurch

6. University of Otago, Dunedin

7. Waitemata District Health Board, Auckland

8. Counties Manukau District Health Board, Auckland

9. Bay of Plenty District Health Board, Tauranga

10. Northland District Health Board, Whangarei

11. Mid Central District Health Board, Palmerston North

12. Waikato District Health Board, Hamilton

13. Southern District Health Board, Dunedin

Background: NETwork! is a multi-faceted clinical and translational research program, that includes a retrospective epidemiological study of neuroendocrine tumours (NETs) in NZ. Previous epidemiological descriptions of NETs are derived from institutional series or regional registries. We report initial data from this study, which includes every NET diagnosed in NZ over a 5-year period.

Methods: Patients diagnosed with NETs from 2008-2012, excluding pulmonary small cell carcinoma. Primary data source was the New Zealand Cancer Registry (NZCR) searched using ICD-03 codes. Secondary data was obtained from searches of pathology records in every hospital in NZ. Clinical data on each case was collected from inspection of individual medical records by data managers across multiple sites.

Results: 1746 patients were diagnosed with NET between 2008 and 2012, giving a crude incidence rate of 7.9 per 100,000 in 2008 steadily increasing to 8.6 per 100,000 in 2012. In total, gastroenteropancreatic NETs made up 43.2% of all NETs reported. Other common primary sites include lung (14.4%) and skin (10.8%). The primary site was unable to be identified in many cases (10.9%). A large proportion (44.5%) had either lymph node or distant metastases at diagnosis. Extrapolation to the Australian population suggests over 2000 new cases per year, with over 900 metastatic at diagnosis.

Conclusions: The incidence of NETs may be higher than reported, and is rising. This, coupled with the relatively high proportion of cases that have local or distant metastases, represents a larger disease burden than currently perceived. We believe this is the first true analysis of NET incidence conducted on a whole population internationally, and therefore offers a level of accuracy not previously available. This data will guide healthcare funding and delivery for people with NETs.

49

The Cancer Stem-Like Cell Marker SOX2 is Prognostic and May Predict Response to Chemotherapy in Colon Cancer

Timothy J Miller[2, 1], Melanie J McCoy[2, 1], Chidozie C Anyaegbu[2], Kim Cheah[3], Chris Hemmings[1, 3], Max K Bulsara[4], Barry Iacopetta[5], Cameron F Platell[2, 1]

1. School of Medicine, University of Western Australia, Perth, Western Australia, Australia

2. St John of God Subiaco Hospital, Subiaco, WA, Australia

3. Australian Clinical Labs, Perth, WA, Australia

4. Institute for Health Research, University of Notre Dame, Fremantle, WA, Australia

5. School of Biomedical Science, University of Western Australia, Perth, WA, Australia

Background: Cancer stem-like cells (CSC) are a sub-population of self-renewing cancer cells that have enhanced tumorigenic capacity. In colon cancer, interactions with tumour-infiltrating lymphocytes can influence the ability of CSC to survive treatment and form secondary tumours. Here we investigated the prognostic value of CSC markers and immune-related markers in stage II/III colon cancer.

Methods: Expression of the putative CSC markers CD133, SOX2, ALDH1, CD44v6 and Lgr5, the T cell markers CD3, CD8 and Foxp3, and programmed death ligand-1 (PD-L1) was assessed in tissue samples from 316 patients with stage II/III colon cancer by immunohistochemistry. Tissue micro-arrays were used and marker expression was digitally quantified using image analysis software. Associations with overall (OS) and cancer-specific (CSS) survival were assessed using Kaplan-Meier estimates and Cox proportional hazards regression.

Results: High SOX2 expression was associated with poor survival (HR, 1.645; [1.01-2.69]; p=0.046) whereas high Foxp3 and high PD-L1 expression were associated with improved survival (HR, 0.48; [0.24-0.98]; p=0.043 and HR, 0.45; [0.22-0.91]; p=0.025 respectively). Patients whose tumours expressed high SOX2 and low PD-L1 had a particularly poor prognosis compared to all other groups (HR, 4.01; [1.81-8.90]; p=0.0006). When cases were stratified based on SOX2 expression, patients with $SOX2^{Low}$ tumours demonstrated a significant benefit from adjuvant chemotherapy (HR, 0.56; [0.32-0.97]; p=0.040) whereas those with $SOX2^{High}$ tumours did not (p=0.973).

Conclusions: These results suggest that SOX2 may be a useful prognostic marker for patients with colon cancer, particularly when the state of the local tumour immune response is taken into account. In this cohort, SOX2 was strongly associated with benefit from adjuvant chemotherapy, supporting further investigation of this CSC marker as a predictor of chemotherapy response.

99

Chemoradiotherapy with capecitabine versus 5-fluorouracil for locally advanced rectal cancer: efficacy in real-world practice

Christine Semira[1], Cameron Platell[2], Margaret Lee[1, 3, 4], Ravish Jootun[2], Suzanne Kosmider[3], Jeanne Tie[1, 3], Rachel Wong[1, 4], Jin Cho[5], Ian Jones[6], Malcolm Steel[7], Peter Gibbs[1, 3]

1. Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria, Australia

2. Colorectal Surgical Unit, St. John of God Subiaco Hospital, Perth, Western Australia, Australia

3. Medical Oncology, Western Health, Footscray, Australia

4. Medical Oncology, Eastern Health, Box Hill, Australia

5. Department of Surgery, Western Health, Footscray, Australia

6. Department of Surgery, Royal Melbourne Hospital, Parkville, Australia

7. Department of Surgery, Eastern Health, Box Hill, Australia

Background: The MARGIT and NSABP-04 trials have demonstrated the equivalence of capecitabine (CAP) and 5FU in the neoadjuvant treatment of locally advanced rectal cancer (LARC) in the context of a randomised clinical trial. However, in routine clinical care, uncertainty regarding patient compliance and inconsistency in CAP prescribing can potentially compromise the efficacy of CAP treatment. Pathologic complete response (pCR) is considered to be a surrogate of treatment efficacy in LARC. **Methods**: This retrospective cohort study analysed routine patient data from multiple sites in Victoria and Western Australia from 2014-2016. Information regarding pCR rates, progression free survival (PFS) and overall survival (OS) for patients with LARC cancer treated with neoadjuvant chemoradiation were obtained from prospectively collected registry data. Chi-square test was done to determine significant differences in pCR. Kaplan-Meier analysis was conducted to obtain PFS and OS**. Results**: A total of 276 LARC patients who received neoadjuvant CAP (n=81; 29%) or 5FU (n=195; 71%) plus radiotherapy were identified. The use of CAP increased over time, with 4% (n=4) of CAP patients treated in 2014, 14.5% (n=40) in 2015 and 13.4% (n=37) in 2016. There were no significant differences between CAP versus 5FU treated patients for age (median 63.3 vs 63.6 years, p=0.59), tumour location (low rectal cancers 60% vs 56%, p=0.84 , or ASA score (ASA 1 60.4 % versus 62.5 %, p=0.09). Fifteen patients (18.5%) in the CAP group versus 49 (25%) from the 5FU group had a pCR (p=0.24). OS and PFS data are still not mature enough to derive meaningful statistics but will be presented. **Conclusion**: In the routine care setting for LARC there is modest uptake of CAP at the sites examined, with chemotherapy treatment selection not clearly influenced by patient factors. The percentage of patients achieving a pCR with 5FU or with CAP appears similar. It will be worth revisiting survival data in the future to see whether the choice of chemotherapy will impact on PFS or OS.

100

First-line EGFR vs VEGF inhibitors in metastatic colorectal cancer: patterns of use from 2009-2017

Christine Semira[1], Kathryn Field[2, 3], Margaret Lee[1, 4, 5, 3], Belinda Lee[1, 2, 3], Louise Nott[6], Jeremy Shapiro[7], Rachel Wong[1, 5], Jeanne Tie[1, 4, 2], Ben Tran[1, 2], Gary Richardson[7], Allan Zimet[8], Lara Lipton[7], Babak Tamjid[9], Matthew Burge[10], Brigette Ma[11], Julie Johns[1], Michael Harold[1], Peter Gibbs[1, 4, 3]

1. Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria, Australia

2. Medical Oncology, Royal Melbourne Hospital, Parkville, Australia

3. The University of Melbourne, Parkville, Australia

4. Medical Oncology, Western Health, Footscray, Australia

5. Medical Oncology, Eastern Health, Box Hill, Australia

6. Royal Hobart Hospital, Hobart, Australia

7. Cabrini Health, Malvern, Australia

8. Epworth Hospital, Richmond, Australia

9. Goulburn Valley Health, Shepparton, Australia

10. Royal Brisbane Hospital, Brisbane, Australia

11. Department of Clinical Oncology, Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, SAR

Background: In follow-up to our 2016 study, we continue to examine patterns of use of EGFR inhibitors (EGFRi) and bevacizumab in the first line treatment of metastatic colorectal cancer (mCRC). **Methods**: This project utilized the Treatment of Recurrent and Advanced Colorectal Cancer (TRACC) database, which captures information regarding mCRC patients receiving care in major hospitals across Australia and now in Hong Kong. Patient demographics, treatment details and survival outcomes were documented and analysed. Kaplan-Meier survival analysis was performed to obtain PFS and OS. **Results**: From 2009 to 2017, 2109 mCRC patients were entered into the TRACC registry, of whom 942 (45%) received a biologic agent as part of 1st line treatment. This was given with an oxaliplatin-based chemotherapy backbone in 680 (72%). The majority (n=911) were given bevacizumab; 31 (1.5%) had an EGFRi (cetuximab=27, panitumumab=4). When comparing biologic treated patients to the overall TRACC population, a similar proportion were male (57.0 vs 58.5%), ages were similar (median age 67.5 vs 67.5 years) as was the proportion that were ECOG 0-1 (80.0% vs 81.9%). Overall the use of EGFRi has slowly been increasing since 1st line PBS funding in mid-2015, with a trend since mid-2016 for use only in left-sided primary tumours. Over the duration of the TRACC registry, the use of anti-VEGF has been stable at 44-50% of the total number of new metastatic patients per year. Median PFS is 19.7 months and 24.08 months respectively for bevacizumab and EGFRI-treated patients; median OS for bevacizumab-treated patients is 26.74 months, and was not reached for EGFRi-treated patients. Any differences were not statistically significant (OS p-value=0.5; PFS p-

value=0.20). **Conclusions**: Over the years, bevacizumab has been consistently used in around half of the patients diagnosed with mCRC. The use of EGFRis is steadily increasing over time. Updated and detailed data will be presented.

Disclosure: This study is supported by Roche Products, Pty. Limited (Australia); Roche has provided financial assistance for the development, installation and maintenance of the TRACC clinical database.

101

Exploring the relationships between physical and psychological symptoms and quality of life in people living after colorectal cancer.

Barbara A Mullan[1], Haryana Dhillon[2], Grace McKie[1], Dominika Kwasnicka[1], Sim Yee (Cindy) Tan[3], Julie Marker[4]

1. Curtin University, Perth, WA, Australia

2. Centre for Medical Psychology & Evidence-based Decision-making, University of Sydney, Sydney

3. Concord Cancer Centre and Nutrition & Dietetics Department, Concord Repatriation General Hospital, , SYDNEY

4. Cancer Voices South Australia, Adelaide

Introduction: Australia has one of the highest rates of colorectal cancer in the world, with nearly 15,000 new cases of colorectal cancer in 2012. Survival rates have increased over the past decade with nearly 70% of individuals who are diagnosed with colorectal cancer likely to survive five years post-diagnosis. Many people live long after their colorectal cancer diagnosis and treatment. Evidence suggests only a third of people reported receiving dietary advice after colorectal cancer and indicate they would be receptive to clear dietary recommendations. They also reported facing barriers to adherence to healthy diets and lifestyles, including comorbidity with other health issues. A systematic review which examined quality of life amongst long term survivors found higher levels of depression, lower physical health and increased distress. Therefore the aim of this research was to qualitatively explore the relationships between physical and psychological symptoms and quality of life in people living after colorectal cancer.

Methods: People living after colorectal cancer were recruited via self-referral or by their treatment team. A semi-structured interview schedule was used. After verbatim transcription a thematic analysis was used to code the data into themes.

Results: Key themes identified included; conflicting advice from different sources, strategies for managing symptoms, changes to diet pre and post diagnosis to manage symptoms, complementary and alternative therapy and frustration with symptoms.

Conclusions: People living after colorectal cancer face multiple challenges and barriers to adopting a healthy lifestyle. The data also provide suggestions for intervention points for dietary changes in this population.

46

Three distinct genomic landscapes define clinical outcome of pancreatic neuroendocrine tumours (pNETs)

Cherie Blenkiron[1], Kate Parker[1], Peter Tsai[1], Sandra Fitzgerald[1], Paula Shields[1], Mee Ling Yeong[2], Nicole Kramer[2], Tamsin Robb[1], Sarah James[1], Mik Black[3], Vicky Fan[1], Nooriyah Poonawala[1], Patrick Yap[4], Esther Coats[1], Brayden Woodhouse[1], Reena Ramsaroop[5], Masato Yozu[6], Bridget Robinson[7], Kimiora Henare[1], Jonathan Koea[8], Peter Johnston[9], Richard Carroll[10], Saxon Connor[11], Helen Morrin[12], Marianne Elston[13], Christopher Jackson[3], Papaarangi Reid[1], John Windsor[1], Andrew MacCormick[14], Richard Babor[14], Adam Bartlett[1], Dragan Damianovich[15], Nick Knowlton[1], Sean Grimmond[16], Michael Findlay[1], Cristin Print[1], Benjamin Lawrence[1]

1. University of Auckland, Auckland, New Zealand

2. Pathology, Auckland District Health Board, Auckland, New Zealand

3. Otago University, Dunedin, Otago, New Zealand

4. Clinical Genetics, Auckland District Health Board, Auckland, New Zealand

5. Pathology, Waitemata District Health Board, Auckland, New Zealand

6. Pathology, Counties Manukau District Health Board, Auckland, New Zealand

7. Medical Oncology, Canterbury District Health Board, Christchurch, New Zealand

8. Surgery, Waitemata District Health Board, Auckland, New Zealand

9. Surgery, Auckland District Health Board, Auckland, New Zealand

10. Endocrinology, Capital Coast District Health Board, Wellington, New Zealand

11. Surgery, Canterbury District Health Board, Christchurch, Canterbury, New Zealand

12. Christchurch Tissue Bank, Otago University, Christchurch, Canterbury, New Zealand

13. Endocrinology, Waikato District Health Board, Hamilton, Waikato, New Zealand

14. Surgery, Counties Manukau District Health Board, Auckland, New Zealand

15. Medical Oncology, Auckland Dstrict Health Board, Auckland, New Zealand

16. University of Melbourne, Melbourne, Victoria, Australia

Background: pNETs are a poorly understood cancer with a highly variable clinical outcome. Genomic analysis of pNETs may provide biological insights that guide therapy.

Methods: 69 sporadic well-differentiated pNETs from 60 individuals along with matched normal tissues underwent deep hybridization capture DNA sequencing of 638 genes and Affymetrix RNA microarrays. More in-depth genomic analysis was undertaken for 12 pNETs including low coverage whole genome sequencing, RNAseq analysis, methylation microarray analysis and microRNA expression microarray analysis. Careful clinical annotation was conducted for each case, then cases de-identified prior to linking with genomic findings. Clinically relevant findings were returned to the patient's physician if deemed appropriate by an incidental findings committee, for patients who consented.

Results: Clustering analysis of copy number changes defined three groups of pNETs with distinct clinical outcomes. pNETs in group 1 (n=11) showed a recurrent pattern of LoH affecting the same 10 chromosomes, in the context of somatic *MEN1* mutation, and often coupled with mutations in genes affecting genome integrity (*ATRX*, *DAXX PTEN*, *MSH2* and *TP53*). Outcomes were unfavourable in this group; 5 of the 11 tumours metastasized, three patients progressed during the study, and 10 had lymphovascular invasion. There was *MGMT* loss through apparent haploinsufficiency which may favour the use of temozolomide. pNETs in group 2 (n=17) also showed *MEN1* mutation and chromosome 11 LoH, but few other chromosomal copy number changes or mutations. This group had favourable outcomes; no patients metastasized, 16 were low grade (Ki-67 <2%), all had low expression of proliferation-associated RNAs and only three had LVI. By contrast, group 3 (n=18) was characterized by absence of *MEN1* gene mutation, contained tumours with variable patterns of aneuploidy (ranging from none to extensive) and pNETs in this group had intermediate outcomes.

Conclusions: The clinical outcome of pNETs is related to a combination of somatic *MEN1* mutation, changes in copy number at a chromosomal level, and mutations in genes related to genome integrity. Implications for selection of therapy will be discussed, including surgery and choice of chemo- and targeted therapy.

48

Fluoropyrimidine-associated myocardial toxicity is a global metabolic effect not vascular spasm and is visible on FDG PET scanning.

Andrew Dean[1], Dominic Higgs[1], Peter Robins[1], Paul Stobie[1], Philip Craven[1], Ciara Daly[1], Samantha Carija[1]

1. St John of God Subiaco, Subiaco, WA, Australia

Background: Myocardial toxicity from fluoropyrimidines is a rare but potentially serious side effect, estimated by some as occurring in up to 9%. Coronary spasm has been suggested as the underlying mechanism, despite a lack of supporting evidence and other toxicity mechanisms have been proposed. Matsubara described Krebs cycle dysfunction in the presence of 5FU with depletion of high energy phosphate compounds in rodent myocardial tissue with ECG changes. Following a chance discovery of abnormal myocardial FDG uptake on a PET scan shortly after presenting with presumed 5FU cardiac toxicity (angina, ST elevation, troponin rise; normal coronary vessels on imaging), we prospectively evaluated all instances of angina occurring during 5FU infusion with coronary artery imaging and FDG PET scan. Methods: We identified 5 patients who experienced angina during 5FU therapy. They were investigated for coronary ischaemia and also underwent PET scanning to assess myocardial FDG uptake. Data was collected from patient records, and subsequent cardiac investigations. Results: In all 5 cases, PET scan demonstrated markedly abnormal FDG uptake throughout the myocardium, with the ventricular blood pool demonstrating more FDG activity than myocardium. No significant underlying coronary artery disease was identified. All 5 patients had previous PET scans with normal myocardial FDG uptake. Conclusions: We identified a consistent pattern of abnormal FDG uptake throughout the myocardium for all scanned patients with chest pain following administration of 5FU. This was not restricted to a single arterial territory. There were no typical ECG changes of spasm. Obstructive coronary disease was excluded with angiographic imaging or myocardial perfusion scanning. The FDG PET scans suggest global myocardial metabolic change, supporting the notion of 5FU being a direct myocardial toxin inhibiting myocardial glucose utilization. The myocardium may then be dependent on fatty acid metabolism, posing additional risk to patients on low fat diets. Our data provides new insight into the mechanism of 5-FU myocardial toxicity and further prospective assessment using PET is warranted.

102

Modified FOLFIRINOX (mFOLFIRINOX) as second-line chemotherapy in pancreatic adenocarcinoma.

Andrew Dean[1], Dominic Higgs[1], Alex James[1], Tegan Van Gemert[1], Alenia T James[1]

1. St John of God Subiaco, Subiaco, WA, Australia

Background: FOLFIRINOX is a highly effective combination chemotherapy regimen with the reputation of only being tolerable to young patients with good performance status. As the original ACCORD study was carried out at specific French university hospitals with patients performance status 0 or 1 many oncologists feel uncomfortable administering mFOLFIRINOX as a second-line therapy. We have previously reported our experience in 24 patients ages 27 - 84 where we concluded that dose modified FOLFIRINOX can be safely administered to elderly patients with appropriate initial dose reductions and subsequent escalation. There is a lack of consensus on a standard second-line regimen for metastatic pancreatic cancer. We conducted a review of dose intensity and outcome for all patients treated with 2nd or 3rd-line mFOLFIRINOX for pancreatic adenocarcinoma at St John of God Hospital, Subiaco, Western Australia in order to assess efficacy and tolerability Methods: Electronic records were used to identify 35 patients who had received 1st-line gemcitabine-based chemotherapy who then went on to receive 2nd or 3rd line mFOLFIRINOX. Case files, laboratory and radiology records were then examined to determine outcomes and toxicities. Results: 35 patients were identified with an age range of 27- 85, both locally advanced and metastatic disease, with 12 over the age of 70. All patients except 2 had gemcitabine plus abraxane in the first line setting. Dose intensity was 65% for oxaliplatin, 68% for irinotecan, 18% for bolus 5-FU and 68% fir infusional 5FU. Toxicity was acceptable with a grade 3 toxicity rate of 10%. Overall survival in this group ranged from 5-67 months (median 23 months for locally advanced / 15 months for metastatic). Notably, 20 patients received greater than 6 cycles of treatment and 8 patients received more than 12 cycles. One patient has received 70 cycles. Conclusions: Our experience demonstrates the safety, tolerability and efficacy of mFolfirinox as a second-line therapy after gemcitabine failure. The disease control rate, even with the reduction in dose intensity, suggests that modified Folfirinox should be formally tested in the 2nd line setting in a clinical trial.

103

Resecting the unresectable - long course gemcitabine/nab-paclitaxel followed by chemoirradiation to downstage locally advanced pancreatic adenocarcinoma

Andrew Dean[1], Dominic Higgs[1], Ian Yusoff, Mikael Johansson, Colin Tang, Rohen White, Dev Segarajasingam , Jeremy Tan, Spiro Raftopoulous , Daniel Venetz, Samarth Rao, Jon Herron, Kevin Jasas, Nigel Spry

1. St John of God Subiaco, Subiaco, WA, Australia

We have previously reported our initial experience with prolonged initial chemotherapy with gemcitabine/abraxane followed by radiotherapy with concurrent infusional 5-FU. Continued application of this treatment approach has now resulted in 18 patients with unresectable pancreatic adenocarcinoma being resected (17 achieving R0 resections) with significantly prolonged survival times. Patients with tri-modality therapy showed a 45% four year survival. An electronic database search was carried out to identify all cases of locally advanced pancreatic cancer treated between 2 institutions. Case records, pathology, radiology and multidisciplinary team meeting records were then examined to determine type and dose of chemotherapy given together with radiological, pathological and survival outcomes. Patients were deemed unresectable if at multidisciplinary team meeting, they were shown to have vascular involvement >180 degrees and considered by the surgical, endoscopic ultrasound and radiological team to be not suitable for vascular reconstruction. Patients were then treated with up to 8 cycles of gemcitabine plus nab-paclitaxel followed by external beam radiotherapy 54Gy in 30 fractions. Follow-up with tumour markers and serial CT scanning was used to determine response and case records were examined for follow-up and survival data. 89 patients were identified who fulfilled these criteria. 18 patients responded well enough to be deemed resectable at subsequent MDT meetings. These patients underwent Whipple's pancreatico duodenectomy. 3 pathological complete responses were seen and 17 of 18 patients achieved an R0 resection. Toxicity was related mainly to neuropathy from oxaliplatin and cytopenia. No treatment related deaths were seen. Medium length of stay following surgery was 18 days and there were no perioperative deaths. Median survival for those receiving or 3 modalities of therapy was greater than 2 years compared to less than 2 years for those not undergoing surgery and 10 months for those not undergoing surgery or proceeding with radiotherapy. Our data suggests that prolonged initial chemotherapy with up to 8 cycles of gemcitabine / nab-paclitaxel followed by radiotherapy with concurrent infusional 5-FU results in a significant number of patients being down staged from unresectable to resectable. Those undergoing tri-modality therapy have particularly impressive survival times.

104

Colorectal T4a tumours - identifying and treating patients at risk of peritoneal metastases

David L Morris[1], Sarah J Valle[2], Nayef A Alzahrani[1], Winston S Liauw[3], Andrew C Lynch[4], Paul Moroz[4]

1. Department of Surgery Peritonectomy Unit, St George Hospital, Kogarah, NSW, Australia

2. Department of Surgery, St George Hospital , Kogarah, NSW , Australia

3. Cancer Care Centre, St George Hospital, Kogarah, NSW, Australia

4. Colorectal Department, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

Colorectal cancer is a priority health concern in Australia with peritoneal being the second most common recurrence site [1] Risk factors for colorectal peritoneal metastases (CRPM) include stage T4a at an occurrence of up to 60% [2]. CRPM are relatively resistant to systemic chemotherapy, even with the use of modern and targeted biological agents [3] resulting in eventual mortality with almost no patients surviving 5-years. The single potentially curative treatment option, only suitable for a small number of patients with no distant metastases and a low volume of tumour, is cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). The extent of PM, however, is a limiting factor for the efficacy of CRS/HIPEC. Many patients are diagnosed with advanced disease where this treatment is no longer of value. In patients presenting with CRPM that undergo CRS/HIPEC, 5-year survival ranges from 15-50% [4,5]. An ideal treatment option would entail early intervention, prior to development of PM or when disease volume is limited.

In previous attempts to prevent CRPM, HIPEC has been given in both the prophylactic and second-look setting following resection of the primary tumour in patients with no evidence of recurrence. These studies reported early intervention with intraperitoneal chemotherapy reduced the rate of recurrence and showed a benefit in overall survival [6-9]. A criticism, however, is that there would be a proportion of patients that were treated with this extensive intraperitoneal treatment that may never have developed PM.

Therefore, the study proposed and led by our internationally recognised CRS team, in an attempt to identify, diagnose and treat CRPM at an early stage, involves performing an exploratory laparoscopy and peritoneal fluid wash cytology including epithelial cell adhesion molecule (EpCAM), carcinoembryonic antigen (CEA), and fluorescence imaging in all patients with T4a tumours following 3-6 months of adjuvant chemotherapy that have no evidence of disease clinically or radiologically. The rationale of this study is to diagnose early PM or patients with positive peritoneal fluid, with endpoints of three-year disease free survival and volume of tumour in patients found to have disease. We also intend to evaluate the most effective method for early diagnosis.

1. Faron M, Macovei R, Goere D, Honore C, Benhaim L, Elias D. Linear relationship of peritoneal cancer index and survival in patients with peritoneal metastases from colorectal cancer. Ann Surg Oncol. 2016;23(1):114-9.
2. Pelz JO, Chua TC, Esquivel J, et al. Evaluation of the best supportive care and systematic chemotherapy as treatment stratified according to the retrospective peritoneal surface disease severity score (PSDSS) for peritoneal carcinomatosis of colorectal origin. BMC Cancer. 2010; 10:689.
3. Segelman J, Granath F, Holm T, et al. Incidence, prevalence and risk factors for peritoneal carcinomatosis from colorectal cancer. Br J Surg. 2012; 99(5):699-705.
4. Jayne DG, Fook S, Loi C, Seow-Choen F. Peritoneal carcinomatosis from colorectal cancer. Br J Surg. 2002; 89:1545-59.
5. Chua TC, Esquivel J, Pelz JO, Morris DL. Summary of current therapeutic options for peritoneal metastases from colorectal cancer. J Surg Oncol. 2013;107(6):566-73.
6. Klaver YL, Lemmens VE, Nienhuijs SW, Luyer MD, De Hingh IH. Peritoneal carcinomatosis of colorectal origin: incidence, prognosis and treatment options. World J Gastroenterol. 2012; 18(39):5489-94.
7. Honore C, Goere D, Souadka A, Dumont F, Elias D. Definition of patients at high-risk of developing peritoneal carcinomatosis after curative surgery for colorectal cancer. A systematic review. Ann Surg Oncol. 2013; 20:183-192.
8. Elias D, Honore C, Dumont F et al. Results of systematic second look surgery plus HIPEC in asymptomatic patients presenting a high risk of developing colorectal peritoneal carcinomatosis. Ann Surg. 2011; 254(2)289-93.
9. Sammartino P, Sibio S, Biacchi D, et al. Long-term results after proactive management for locoregional control in patients with colonic cancer at high risk of peritoneal metastases. Int J Colorectal Dis. 2014; 29(9):1081-9.

50

Follow-up and recurrence in resected gastroenteropancreatic neuroendocrine tumours: A population-based study

David Chan[1], Eva Segelov[2], Lesley Moody[3], Ning Lui[4], Hadas Fischer[4], Peter Austin[4], Simron Singh[1]

1. Medical Oncology, Sunnybrook Hospital, Toronto, Ontario, Canada

2. Monash Health, Clayton, VIC, Australia

3. University of Toronto, Toronto, Ontario, Canada

4. Institute of Clinical Evaluative Sciences, Toronto, Ontario, Canada

Background: Neuroendocrine tumours (NETs) are uncommon. Little data exist to guide follow-up in resected disease, with no consensus regarding the optimal follow-up frequency or modality. Follow-up imaging regimens

are extrapolated from other gastrointestinal tumours. As NETs are heterogeneous, this may result in both over-use and underuse of investigations in patients.

Methods: A population-based retrospective cohort study using linked data from the Institute for Clinical Evaluative Sciences and the Ontario Cancer Registry (capturing more than 99% of incident cases in Ontario) was conducted to evaluate patients diagnosed with gastroenteropancreatic NETs in Ontario, Canada from 1994 to 2012. Recurrence-free survival and the frequency of cross sectional imaging (abdominal computed tomography (aCT), magnetic resonance imaging (aMRI) and ultrasound (aUS)) were the main outcomes.

Results: Nine hundred and thirty-six patients were identified with median follow-up 47 months. The mean age was 59, 51% were female, and distribution of primary cancers was: small intestine 47%, pancreas 20%, large intestine 21%, rectum 6.4%, stomach 6.0%. The median survival time to a composite outcome of recurrence or death was 7.2 years, and 9.5 years if censoring on death. The cumulative incidence of recurrence was 8.4% (95% CI 6.8% to 10.3%) within one year, 33.7% (95% CI 30.4% to 36.9%) within five years, and 48.5% (95% CI 44.4% to 52.4%) within 10 years. The rate of recurrence significantly increased with age (HR = 1.529 for age 50-70 compared to <50, p=0.0003), pancreatic primary (HR = 1.463, p=0.0006), but not the income quintile (p=0.1071), rurality (p=0.1931) or gender (p=0.3787).

The rate of use of aCTs, aMRIs and aUS decreased over time, from 1.04 per 100 patient-days in months 1-3 to 0.22 at months 49-60. On average, 1.59 abdominal CTs per patient were performed in the first year, 0.83 in the second year and 0.52 in years 3-5.

Conclusions: Unlike colon cancer, significant numbers of NETs recur between 5-10 years after curative surgical resection. These data support the lengthening of follow-up for resected NETs to a minimum of 10 years. Future research should focus on the impact of imaging on early detection of recurrence and survival outcomes.

51

Optimising followup after complete surgical resection of Gastrointestinal Neuroendocrine Tumours- a Delphi process to produce expert consensus in an area lacking clinical evidence

Lesley Moody[1], Eva Segelov[2], David Chan[3], Jonathan Strosberg[4], David Metz[5], Simron Singh[3]

1. University of Toronto, Toronto, Ontario, Canada

2. Monash Health, Clayton, VIC, Australia

3. Medical Oncology, Sunnybrook Hospital, Toronto, Ontario, Canada

4. GI Oncology, Moffitt Cancer Center, Tampa, Florida, USA

5. Medicine, Hospital of the University of Pennsylvania, Philadelphia, USA

Introduction: Optimal follow-up for completely resected GI-NETS has not been well defined, with heterogeneity in awareness and application of existing guidelines. **Aim(s):** To investigate follow-up in GI-NETs using RAND/UCLA appropriateness methodology (RAM). **Materials and methods:** A multidisciplinary expert panel (n=18) scored 193 follow up care scenarios for GI-NETS using an online survey. Appropriateness of schedules and investigations for follow up were scored from 1 to 9. Median appropriateness scores were considered. Consensus was reached when 75% scored the scenario similarly. **Results:** Significant variation in followup duration and intensity existed, particularly beyond five years. For both Grade 1 & 2 tumours, followup frequency was impacted by nodal status, size and time since resection. Regardless of site, grade, tumour size or nodal status, cross sectional imaging and blood/urine-based biomarkers were scored as appropriate, whereas uncertainty in appropriateness was recorded for functional imaging. Fully resected, Grade 1 appendiceal NET, size <1cm was deemed appropriate to never follow up; but if 1-2 cm, there was uncertainty about frequency but certainty in the use of CT and biomarkers. Fully resected, Grade 1, T1 rectal NET was scored appropriate to followup once at 12 months with sigmoidoscopy, then discharge from followup. **Conclusion:** Using RAM, we describe appropriate followup frequency and necessary tests for follow up care of patients with fully resected GI-NETS. Areas of uncertainty requiring more study were identified