planned (p = 0.001). Of pts who required UHA, only 27% resumed their trial drug after recovery. The main statistically significant risk factors for UHA include >2 metastatic sites, (RR 2.6 [1.64–4.38], p = 0.001), poor performance status (RR 2.47 [1.48–3.72] p = 0.003), low albumin (RR 2.17 [1.36–3.52] p = 0.001) and cytotoxic combination trials (RR 1.7 [1.09–2.86] p = 0.025).
Conclusions: Unplanned admissions constitute 20.6% of Phase I inpatients, with the majority being disease rather than treatment-related. Regardless of length of stay, UHA portend poor outcomes for patients who are on treatment, with a risk profile underscoring the importance of pt and trial selection.

1258 POSTER

Changing perceptions of oncologists referring advanced colorectal (ACRC) patients (pts) to phase 1 trials: an evidence based approach

A.T. Brunetto[1], D.S.W. Tan[1], D. Olmos[1], T. Yap[1], S. Frentzas[1], S. Sandhu[1], K. Denholm[1], B. Ayite[1], J. de Bono[1], S. Kaye[1]. *[1]Institute Cancer Research, Drug Development Unit, London, United Kingdom*

Introduction: After failure of conventional treatment pts with ACRC who remain well may receive phase 1 therapy. Pts rely on referring physicians opinion when considering treatment and a change in perception may increase number of referrals.
Methods: Analyze the outcome for 78 ACRC pts treated in 23 phase I trials at the Royal Marsden Hospital (RMH), between Jan 04–08. Apply newly developed RMH prognostic score (0−3, comprising high LDH, albumin <35 mg/dl and $\geqslant$2 number of metastatic sites; In addition, survey 64 colorectal oncologists who referred pts to our unit aiming to understand the reasons for referral and knowledge regarding experimental therapy. Describe whether after reading audit results their approach to phase 1 changed.
Results: *Audit*: Median age:62 yrs [range (r):26–79]. PFS and OS were 8.6 (95% CI: 6.4–10.7) and 29.1 weeks (95% CI: 15.7–42.5), respectively. 28.8 and 8.2% of the pts were assessed as having SD at 3 and 6 months, respectively. In the multivariate analysis, a high RMH prognostic score (2−3) was associated with poor OS [HR: 1.42 (1.09–1.85), p = 0.007]; median OS was 19.4 weeks (95% CI 11.7–27.1) compared to 47.4 weeks for those pts with RMH prognosis score of 0–1 (95% CI 41.3–53.6, p = 0.029).
Survey: 28/64 (44%) questionnaires were returned from medical and clinical oncologists (14/14). The median length of oncology experience was 10 yrs (r: 2−25); 64% had previous phase 1 experience and >85% were familiar with logistics and eligibility criteria. The most common reason for referral was lack of treatment options (64%); and the main reason for referral to our unit was proximity to pts (32%) and known centre of excellence (29%). The most common characteristic analyzed in pts before referral was performance status (93%). Median time spent with pts to discuss phase 1 was 10min (r:5−45) and possibility of any clinical benefit (43%) the main point. The median predicted PFS and OS was 2 (r: 2−4) and 5 (r: 4−8) months, respectively. 39% predicted that the prognostic factors in RMH score would be associated with outcome. 68% felt the audit results met their expectations although 42% would change their approach in some way. Moreover 21% would increase the number of referrals and 81% would be keen to answer similar questionnaires in the future.
Conclusion: Colorectal oncologists have a good knowledge regarding general outcomes of phase 1 trials in ACRC. The most common reason for referral was lack of treatment options, 42% of oncologist surveyed would change their approach in some way after reading audit results and 1/5 would increase their number of referrals.

1259 POSTER

Trabedersen (AP 12009) in the treatment of pancreatic carcinoma and other malignant tumors: interim results of the Phase I/II study

H. Oettle[1], A. Hilbig[1], T. Seufferlein[2], T. Luger[3], R.M. Schmid[4], G. Von Wichert[5], H. Heinrichs[6], K.H. Schlingensiepen[6]. *[1]Universitätsmedizin Berlin Charité, Campus Virchow-Klinikum, Berlin, Germany; [2]Universitätsklinikum Halle (Saale), Innere Medizin, Halle (Saale), Germany; [3]Universitätsklinik Münster Klinik und Poliklinik für Hautkrankheiten, Klinisches Zentrum für innovative Dermatologie, Münster, Germany; [4]II. Medizinische Klinik und Poliklinik des Klinikums rechts der Isar der Technischen Universität München, Gastroenterologie, München, Germany; [5]Universitätsklinikum Ulm, Innere Medizin I, Ulm, Germany; [6]Antisense Pharma, Clinical Research, Regensburg, Germany*

Background: TGF-β2 stimulates metastasis of various malignant tumors and suppresses antitumor responses of the immune system.
Trabedersen (AP 12009) is a TGF-β2-specific antisense oligonucleotide. Trabedersen was safe and effective in high-grade glioma patients, as shown in a randomized, active-controlled Phase IIb study. In patients with anaplastic astrocytoma the median survival benefit was 17.4 months compared to standard therapy. A Phase III study (SAPPHIRE) is ongoing. In this study we evaluate the maximum tolerated dose (MTD), safety, tolerability, pharmakokinetics, and efficacy of intravenous treatment with trabedersen in patients with other advanced tumors.
Methods: In the open label, multicenter, dose-escalation Phase I/II study (AP 12009-P001; NCT00844064; sponsor: Antisense Pharma, GER), 33 patients with advanced pancreatic carcinoma (stage IVA/IVB, N = 23), malignant melanoma (stage III/IV, N = 5), or colorectal carcinoma (stage III/IV, N = 5) were enrolled in several cohorts. Patients were treated intravenously with trabedersen as 2nd to 4th-line therapy as monotherapy with escalating doses in two treatment schedules (1st schedule: 7 d on, 7 d off; 2nd schedule: 4 d on, 10 d off; up to 10 cycles).
Results: Treatment with trabedersen was safe and well tolerated. Within the 1st treatment schedule MTD was established at 160 mg/m^2/d, after NCI-CTC grade 3 dose limiting toxicities (2 self-limiting and transient thrombocytopenias, 1 exanthema) had occurred. One patient with metastatic pancreatic carcinoma had a complete response of liver metastasis and is alive 41 months after enrollment.
In the 2nd treatment schedule dose escalation was stopped after the 4th cohort, before MTD had been reached, as a dose was identified, which was well tolerated and had very promising efficacy data. The median overall survival for patients with pancreatic carcinoma treated with the defined dose (N = 5) was 13.4 months. One patient of this cohort shows stable disease 14.8 months after enrollment in the study.
First efficacy results were also seen in advanced malignant melanoma, as one patient treated within the 1st schedule survived 13.8 months.
Conclusions: Trabedersen is a promising treatment option for patients with advanced solid tumors. Currently the study continues with recruitment of 24 patients with either pancreatic carcinoma or malignant melanoma.

1260 POSTER

Multicenter parallel phase II trials of the polo-like kinase 1 inhibitor BI-2536 in patients with advanced head and neck cancer, breast cancer, ovarian cancer, soft tissue sarcoma and melanoma. The first protocol of the European Organisation for Research and Treatment of Cancer (EORTC) Network Of Core Institutes (NOCI)

P. Schöffski[1], J.Y. Blay[2], J. De Greve[3], E. Brain[4], J.P. Machiels[5], J.C. Soria[6], S. Sleijfer[7], G. Munzert[8], J. Rapion[9], D. Lacombe[9]. *[1]U.Z. Gasthuisberg, Department of General Medical Oncology, Leuven, Belgium; [2]Centre Leon Berard, Department de Medecine, Lyon, France; [3]Universitair Ziekenhuis Brussel, Department of Medical Oncology, Brussels, Belgium; [4]Centre Rene Huguenin, Medical Oncology, Saint-Cloud, France; [5]Cliniques Universitaires St. Luc, Medical Oncology Unit, Brussels, Belgium; [6]Institut Gustave Roussy, Department of Medicine, Villejuif, France; [7]Erasmus University Medical Center, Department of Medical Oncology, Rotterdam, The Netherlands; [8]Boehringer Ingelheim, Clinical Research, Biberach, Germany; [9]European Organisation for Research and Treatment of Cancer, Headquarters, Brussels, Belgium*

Background: BI-2536 inhibits Polo-like kinase 1 (Plk1), resulting in mitotic arrest, disruption of cytokinesis, and apoptosis in susceptible tumor cell populations. Plk1, a serine/threonine-protein kinase, is a key regulator of multiple processes fundamental to mitosis and cell division. EORTC 90061 assessed the efficacy and safety of BI-2536 in five different cohorts of patients with advanced solid tumours.
Materials and Methods: Patients with head and neck cancer (no prior chemotherapy [CTX] for recurrent or metastatic disease), breast cancer (after a maximum of two lines of prior CTX), ovarian cancer (progressive within 6 months after completion of platinum based CTX), soft tissue sarcoma (after no more than one combination or two single agent CTX) or CTX-naïve melanoma with documented progression, adequate performance status, and good organ function were eligible. BI-2536 was given by i.v. infusion of 200 mg on day 1 every three weeks until intolerance or disease progression. Primary end point was the objective response rate (OR) according to RECIST. Secondary end points included safety (CTCAE version 3.0) and overall survival. For each tumour type a Simon optimal 2-stage design for OR was applied (type 1 and type 2 error 10%, null hypothesis 5% OR, alternative hypothesis 20% OR; stage 1 and 2: 12 and an additional 25 patients, respectively). If no OR were observed among the first 12 patients the tumour type was closed for further accrual.
Results: 76 patients were included between 07/2007 and 04/2008. Five patients never received study drug because of ineligibility. The median number of cycles was 2 in all organ types, except for a median of 4 in ovarian cancer. Main drug-related toxicities were febrile neutropenia (gr 3/4: 19.7%), and fatigue (gr 2/3: 31.0%). Most frequent grade 3−4 toxicities were neutropenia (81.6%), thrombocytopenia (19.7%) and anemia (15.5%). Most frequent non-hematologic toxicities were fatigue (gr 2/3: 31.0%), alopecia (26.7%), anorexia (14.1%), and nausea (12.7%), mostly grade 1−2. An