was found with trabectedin. Similar antitumour efficacy was shown in pts younger and older than 60 years in a multivariate analysis.

9403 ORAL

Eribulin mesylate (E7389) in patients with leiomyosarcoma (LMS) and other (OTH) subtypes of soft tissue sarcoma (STS): a Phase II study from the European Organisation for Research and Treatment of Cancer - Soft Tissue and Bone Sarcoma Group (EORTC 62052)

P. Schöffski[1], J.T. Hartmann[2], P. Hohenberger[3], A. Krarup-Hansen[4], J. Wanders[5], C. Hayward[5], D. Druyts[6], M. Van Glabbeke[7], R. Sciot[7], J.Y. Blay[8]. *[1]University Hospitals Leuven, General Medical Oncology, Leuven, Belgium; [2]Comprehensive South West German Comprehensive Cancer Center Eberhard-Karls-Universität, Oncology and Hematology, Tübingen, Germany; [3]Universitätsmedizin Mannheim, Surgical Oncology and Thoracic Surgery, Mannheim, Germany; [4]Copenhagen University Hospital, X, Herlev, Denmark; [5]EISAI Europe Ltd., London, United Kingdom; [6]EORTC Headquarters, Brussels, Belgium; [7]University Hospitals Leuven, Department of pathology, Leuven, Belgium; [8]Centre Léon Bérard, Department of Medical Oncology, Lyon, France*

Purpose: Eribulin is a synthetic analogue of halichondrin B, a substance derived from a marine sponge (Lissodendoryx sp.). Eribulin binds close to but does not overlap with the vinca domain of tubulin, inhibits tubulin polymerization and forms non-functional tubulin aggregates, resulting in inhibition of mitotic spindle assembly, induction of cell cycle arrest at the G2/M phase and tumor regression in preclinical models. EORTC 62052 assesses the efficacy and safety of eribulin mesylate in four strata of pts with different STS.
Patients and Methods: We report on the completed LMS (39 pts) and OTH (30 pts) strata of this trial. Results on adipocytic and synovial sarcoma will be reported elsewhere. Pts with intermediate or high grade STS who had received no more than two lines of previous chemotherapies (two single agents or one combination) for advanced disease, with documented progression, adequate performance status, and good organ function were eligible. Eribulin mesylate 1.4 mg/m^2 was given over 2−5 min as i.v. bolus on days 1 and 8 every three weeks until intolerance or disease progression. The primary end point was the progression-free rate at 12 weeks (PFR12wks) according to RECIST. Secondary end points included safety, response and time-related parameters. A Simon 2-stage design was applied (P1: 40%; P0: 20%; $\alpha = \beta = 0.1$) for each stratum.
Results: Grade 3−4 drug-related adverse events occurring in >1 pat were leucopenia (34% of pts), neutropenia (51%), anemia (9%), febrile neutropenia (4%), increases in ALAT (3%) and fatigue (3%). One patient died of cerebrovascular ischemia, for which a relationship with eribulin could not be ruled out. The PFR12wks was 32% (12/37 pts) in LMS and 29% (7/24 evaluable pts) in OTH. The median PFS in LMS was 3 mo (95% confidence interval 2−4), the median OS 18 (9-N) mo, with 65% of pts alive at 1 year, which compares favorably to historical controls. The median PFS in OTH was 2 (1−3) mo, the median OS 8 (5−15) mo, with 26% of pts alive at 1 year. Conclusions: Eribulin mesylate is very well tolerated in pretreated pts with defined subtypes of STS, and it deserves further study in LMS. The PFR12wks reached predefined statistical boundaries by the Simon 2-stage design in both LMS and OTH.

9404 ORAL

A Phase II study of cediranib in patients with metastatic gastrointestinal stromal tumours (GIST) and metastatic soft tissue sarcoma (STS) (including alveolar soft part sarcoma [ASPS])

K. Gardner[1], I. Judson[1], M. Leahy[2], E. Barquin[1], M. Marotti[3], B. Collins[3], H. Young[3], M. Scurr[1]. *[1]Royal Marsden Hospital, London, United Kingdom; [2]The Christie Hospital, Manchester, United Kingdom; [3]AstraZeneca, Alderley Park, Macclesfield, United Kingdom*

Background: Cediranib (RECENTIN™) is an oral highly potent VEGF signalling inhibitor of all three VEGF receptors. The primary objective of this open-label, two-centre study was to assess the antitumour activity of cediranib in patients with GIST using FDG-PET (standardized uptake value, SUV_{max}). Secondary objectives included assessments of objective tumour response (RECIST), and safety and tolerability in both GIST and STS.
Methods: Patients with histologically or cytologically confirmed GIST resistant or intolerant to imatinib, or metastatic STS refractory to standard therapies or for which no standard therapy existed, received cediranib 45 mg/day (ClinicalTrials.gov Identifier NCT00385203; AZ 2171IL/0046). The primary analysis was performed after all patients had received 16 weeks of treatment and had undergone a week 16 scan for RECIST assessment or had withdrawn from the study before week 16.
Results: Thirty-six patients were enrolled and 34 received treatment with cediranib with a mean daily dose of 36 mg (GIST: n = 24 [13 of whom had previously received sunitinib following imatinib]); STS: n = 10, including ASPS: n = 6). In the GIST patients, FDG-PET showed no significant change from baseline in mean SUV_{max} at days 8 or 29. Some partial metabolic responses were observed in individual patients (Table). Best objective response (RECIST) in the GIST patients showed a 62% stable disease (SD) rate (Table), including 10 patients with SD >16 weeks. There was some evidence of antitumour activity in patients with STS, particularly in the six patients with ASPS (PR, n = 3; SD, n = 3 [including 2 patients with SD >16 weeks]). The most common adverse events (GIST; STS) were diarrhoea (n = 18; n = 6), fatigue (n = 15; n = 7) and hypertension (n = 17; n = 3).
Conclusions: This ongoing study has provided evidence of activity with cediranib monotherapy in some patients with second- and third-line GIST as measured by FDG-PET and SD >16 weeks. In patients with metastatic ASPS, cediranib showed evidence of antitumour activity by RECIST and further investigation in this disease is warranted. The overall safety profile was consistent with previous cediranib studies.

	GIST (n = 24)	
	Day 8 (n = 22)	Day 29 (n = 20)
FDG mean % change from baseline in SUV_{max} (95% CI)	6.8%(−19.95, 33.54)	4.6% (−8.05, 17.34)
FDG tumour response, n	Day 8 (n = 24)	Day 29 (n = 24)
Partial metabolic response (PMR, SUV decrease ⩾25%)	3*	4
Stable metabolic disease (SUV increase ⩽25% or decrease <25%)	16	12
Progressive metabolic disease (SUV increase >25%)	3	4
Non-evaluable	2	4

*Including 1 unconfirmed PMR

Best overall response (RECIST), n	GIST (n = 24)	STS	
		ASPS(n = 6)	Other (n = 4)
CR	0	0	0
PR	0	3	0
SD	15	3	1
Progressive disease	5	0	1
Non-evaluable	4	0	2

9405 ORAL

Spectrum of KIT and PDGFRA mutations in primary gastrointestinal stromal tumours: Polish clinical GIST registry experience

A. Wozniak[1], P. Rutkowski[2], M. Debiec-Rychter[3], J. Siedlecki[4], W. Michej[5], C. Osuch[6], M. Matlok[7], W. Ruka[2], J. Limon[1]. *[1]Medical University of Gdansk, Department of Biology and Genetics, Gdansk, Poland; [2]Sklodowska-Curie Cancer Institute, Department of Soft-Tissue/Bone Sarcoma and Melanoma, Warsaw, Poland; [3]Catholic University of Leuven, Center for Human Genetics, Leuven, Belgium; [4]Sklodowska-Curie Cancer Institute, Department of Molecular Biology, Warsaw, Poland; [5]Sklodowska-Curie Cancer Institute, Department of Pathology, Warsaw, Poland; [6]Jagiellonian University, Dept of Surgery, Cracow, Poland; [7]Jagiellonian University, Department of Surgery, Cracow, Poland*

Background: *KIT* or *PDGFRA* gene mutations are found in 80−90% of gastrointestinal stromal tumors (GIST). The prognostic value of those mutations for the outcome in primary tumours is controversial. Objective: To assess the spectrum, frequency and prognostic significance of the *KIT* and *PDGFRA* gene mutations in Polish group of surgically treated primary GISTs.
Materials and Methods: DNA isolated from paraffin blocks from 300 patients (pts) with histologically diagnosed primary GISTs included in clinical registry database, were analyzed using denaturing high performance liquid chromatography DNA isolated from paraffin blocks from 300 patients (pts) with histologically diagnosed primary GISTs included in clinical registry database, were analyzed using denaturing high performance liquid chromatography (DHPLC) and direct sequencing for *KIT* (exons 9, 11, 13, 17) and *PDGFRA* (exons 12, 14, 18) mutations. For primary GIST risk assessment the Miettinen stratification was used.
Results: *KIT*/*PDGFRA* genes mutations were found in 82% tumours: *KIT* was mutated in 69% and *PDGFRA* in 13%/genes mutations were found in 82% tumors: was mutated in 69% and in 13% of tumors. *KIT* exon 11 and 9 mutations were found in 61.5% and 7.5% respectively. Among *KIT* exon 11 mutants the most frequent were deletions (32.7%) followed by point mutations (15.3%), duplications (8.4%) and complex rearrangements (5.1%). *KIT* exon 11 mutations were found at the similar rates in tumours with gastric and nongastric localization (53.9% vs. 46.1% respectively) while *KIT* exon 9 duplications were more often observed in nongastric GISTs (86.4%, p = 0.00036) and *PDGFRA* mutations were more frequently found in tumours originated from the stomach (86.8%; p = 0.00017). In high