	G 3/4 ALT increases in Cycle 1–2		*p* value*
	Yes	No	
Progression Free Survival (q3w)			
1 line of platinum			
No. of patients (events)	50 (35)	46 (33)	
Median (months)	5.0	6.6	0.6945
>1 line of platinum			
No. of patients (events)	34 (23)	18 (16)	
Median (months)	5.5	6.0	0.8048
1 *vs.* >1 platinum	50 (35) vs 34 (23), 5.0 vs 5.5		0.4673
		46 (33) vs 18 (16), 6.6 vs 6.0	0.7939
Duration of Response (q3w)			
1 line of platinum			
No. of patients (events)	17 (16)	16 (15)	
Median (months)	4.2	5.7	0.4723
>1 line of platinum			
No. of patients (events)	12 (9)	8 (8)	
Median (months)	6.3	5.9	0.9445
1 *vs.* >1 platinum	17 (16) vs 12 (9), 4.2 vs 6.3		0.5009
		16 (15) vs 8 (8), 5.7 vs 5.9	0.8160

*Exploratory log-rank test p-value.

8005 ORAL

MET Amplification is a Molecular Hallmark in Endometriosis-associated Ovarian Clear Cell Carcinoma and Correlates With Worse Prognosis

Y. Yamashita[1], Y. Yatabe[2], S. Akatsuka[1], H. Kajiyama[3], F. Kikkawa[3], T. Takahashi[4], S. Toyokuni[1]. *[1]Nagoya University Graduate School of Medicine, Department of Pathology and Biological Responses, Nagoya, Japan; [2]Aichi Cancer Center Hospital, Department of Pathology and Molecular Diagnostics, Nagoya, Japan; [3]Nagoya University Graduate School of Medicine, Department of Obsterics and Gynecology, Nagoya, Japan; [4]Nagoya University Graduate School of Medicine, Division of Molecular Carcinogenesis Center for Neurological Diseases and Cancer, Nagoya, Japan*

Background: Clear cell carcinoma (CCC) of the ovary is a chemo-resistant tumour with relatively worse prognosis and is frequently associated with endometriosis. Although it is assumed that oxidative stress may have some role in the carcinogenesis of CCC, characteristic molecular events remain obscure.
Materials and Methods: Formalin-fixed, paraffin-embedded tissues from 73 CCC patients and 3 ovarian endometrioid adenocarcinoma (EM) patients of Nagoya University Hospital were obtained. The experimental designs were reviewed and approved by the Committee for Bioethics of Nagoya University Graduate School of Medicine. Array-based comparative genomic hybridization (Array-CGH) analyses using DNA obtained from 13 CCC patients, 3 EM patients and 8 CCC cell lines were performed according to the instructions of Agilent Technologies. Fluorescent in situ hybridization (FISH) was performed using fluorescent labeled probes for MET gene and a control centromere probe. Real-time PCR analysis for copy number change, immunoblotting, immunohistochemistry, and knockdown of the MET gene in CCC cell lines with virally transduced short-hairpin RNA (shRNA) were all performed by standard protocols.
Results: In array CGH, amplification of the chromosome 7q31.31 region frequently less than 2 Mb showing a peak at the MET gene was detected in 4 of the 13 CCC cases, and 2 of the 8 CCC cell lines. Amplification and overexpression of the MET gene was confirmed by FISH, real-time PCR, immunoblotting and immunohistochemistry. MET amplification was not detected in the 3 EM cases. Totally, 37% of the 73 CCC cases had MET amplification detected by real-time PCR analysis. Furthermore, stage 1 & 2 CCC patients with MET amplification (n = 19) had significantly worse prognosis than patients without MET amplification (n = 34) ($p < 0.05$). Finally, knockdown of the MET gene in MET amplified cell lines, JHOC-5 and JHOC-8,resulted in a large decrease in cell viability.
Conclusion: MET amplification is a molecular hallmark in ovarian CCC, and is associated with worse prognosis. MET signaling pathway may have an important role in the carcinogenesis of endometriosis-associated CCC.

8006 ORAL

Prognostic Significance of FOXL2 Mutation and mRNA Expression in Adult and Juvenile Granulosa Cell Tumours of the Ovary

E. D'Angelo[1], A. Mozos[1], D. Nakayama[1], I. Espinosa[1], L. Catasus[1], J. Muñoz[1], J. Prat[1]. *[1]Hospital de Sant Pau Autonomous University of Barcelona, Pathology, Barcelona, Spain*

Background: Recently, mutation of the *FOXL2* gene has been consistently identified in adult granulosa cell tumours of the ovary. The purpose of this study is to investigate whether the *FOXL2* mutation and mRNA expression have a role in the pathogenesis of juvenile and adult granulosa cell tumours and influence tumour progression.
Material and Methods: Thirty-four adult granulosa cell tumours and 20 juvenile granulosa cell tumours were examined for the presence of the *FOXL2* (C402G) mutation. Expression levels were studied by quantitative PCR and immunohistochemistry.
Results: We found that *FOXL2* (C402G) mutation was present in 19/27 (70%) of the adult type tumours but in none of the juvenile granulosa cell tumours (0/18). No correlation was encountered between the presence of *FOXL2* mutation and various clinicopathologic parameters except for the presence of a different sex cord component, which was more frequently found in the subgroup of wild type adult granulosa cell tumours than in the mutated tumours. Patients with tumours harboring the *FOXL2* (C402G) mutation had a worse disease free survival than those with the wild type gene. Expression levels of *FOXL2* mRNA had an impact on disease free survival both in adult and juvenile granulosa cell tumours. We also found that the mutated tumours had a higher immunohistochemical expression of the FOXL2 protein, and there was a linear correlation between mRNA and immunohistochemical FOXL2 expression both in adult and juvenile granulosa cell tumours.
Conclusions: Patients with juvenile granulosa cell tumours and higher FOXL2 protein expression had worse overall survival and disease free survival than those with negative or weakly immunoreactive tumours.
Our data suggest that *FOXL2* mutation and mRNA expression are of prognostic importance both in adult and juvenile granulosa cell tumours.

8007 ORAL

Catumaxomab Induces Efficient Anti-tumour Activity in Vitro With Immune Cells From Ovarian Cancer Patients After Chemotherapy Treatment

I. Braicu[1], J. Atz[2], K. Dettmar[2], H. Martinius[3], R. Spannagl[4], D. Seimetz[5], H. Lindhofer[6], R. Chekerov[7], K. Pietzner[8], J. Sehouli[8]. *[1]Charité Medical University, Department of Gynecology, Berlin, Germany; [2]Fresenius Biotech GmbH, Preclinical Development, Munich, Germany; [3]Fresenius Biotech GmbH, Laboratory, Planegg/Martinsried, Germany; [4]Fresenius Biotech GmbH, Scientific Development, Planegg/Martinsried, Germany; [5]Fresenius Biotech GmbH, CSO, Munich, Germany; [6]TRION Pharma GmbH, Scientific Development, Munich, Germany; [7]Charité, Department of Gynecology, Berlin, Germany; [8]Charité, Department of Obstetrics and Gynecology, Berlin, Germany*

Background: The trifunctional antibody catumaxomab (anti-EpCAM x anti-CD3) is approved in the EU for the intraperitoneal treatment of malignant ascites. Since catumaxomab transiently links immune effector cells to tumour cells resulting in cellular cytotoxicity towards the tumour cells, a functional immune system is essential for effective anti-tumour activity. Consequently, this study investigated the potential influence of chemotherapy treatment of patients with ovarian cancer on the anti-tumour activity of catumaxomab.
Material: Immune cells of patients taken at different time points before and after chemotherapy were used to assess catumaxomab-mediated cytotoxicity *in vitro*. A total of 22 ovarian cancer patients were selected for the analysis. Patients had received carboplatin/paclitaxel (1st-line treatment) or topotecan or doxorubicin monotherapy as 2nd–x-line treatment, respectively. Peripheral blood was collected and purified patient immune effector cells were used to evaluate catumaxomab-mediated cytotoxicity in a co-culture test system with SK-OV-3 ovarian tumour cells as EpCAM+ target cells.
Results: An effective and concentration-dependent anti-tumour activity mediated by catumaxomab was demonstrated using immune effector cells from ovarian cancer patients. For all patient samples efficient elimination of tumour cells was demonstrated at catumaxomab concentrations that correspond to the therapeutic dose range. However, anti-tumour activity *in vitro* varied when comparing patient's immune cells to healthy control PBMC.
Conclusions: This study clearly shows that immune effector cells from ovarian cancer patients undergoing standard chemotherapy can be activated by catumaxomab for efficient killing of EpCAM+ tumour cells. These data provide a scientific basis for the integration of catumaxomab therapy into chemotherapeutic regimens.