

ESMO 2017 Report

Integrating science into oncology for a better patient outcome

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Breast cancer

September 8, 2017

Combined taselisib and letrozole improves response in postmenopausal women with ER-positive, HER-negative early breast cancer: Adding taselisib, a selective PI3-kinase inhibitor with enhanced activity against PIK3CA mutant cancer cells, to letrozole improved the objective response rate in postmenopausal women with early breast cancer overall and in a subset of women with PIK3CA mutant tumours. (LBA10_PR – Saura C, et al.)

Invasive DFS rates following trastuzumab are improved with neratinib over placebo in early stage HER2-positive breast cancer: Invasive disease-free survival (DFS) rates were significantly better in patients with early stage HER2-positive breast cancer treated with extended adjuvant neratinib, although at expense of a transient deterioration of health-related quality of life according to findings from companion studies of a phase III ExteNET trial data. (1490 - Martin Jimenez M, et al.; 177P – Delaloge S, et al.)

Combined letrozole plus palbociclib is not better than chemotherapy as neoadjuvant treatment in luminal breast cancer: Results of the UNICANCER-NeoPAL study did not show improved residual cancer burden or breast conserving surgery rates with a combination of letrozole and palbociclib over third generation chemotherapy as neoadjuvant treatment of women with luminal breast cancer. (LBA9 – Cottu P, et al.)

September 9, 2017

<u>TIL levels signal pembrolizumab response in metastatic TNBC</u>: Patients with metastatic triple negative breast cancer (TNBC) are more likely to show a strong response to pembrolizumab if more tumour infiltrating lymphocytes (TILs) are present in the tumour microenvironment. (LBA13 – Loi S, et al.)

<u>Promising response rates in patients with metastatic TNBC treated with nivolumab after induction treatment</u>: The response rates seen with nivolumab after modulation of the tumour micro-environment using either irradiation or chemotherapy are promising compared to the historical response rates demonstrated in previous PD-1/PD-L1 blockade monotherapy studies in unselected patients with metastatic triple negative breast cancer (TNBC). (LBA14 – Kok M, et al.)

September 10, 2017

Combined abemaciclib with NSAI show significant clinical benefit as initial treatment for patients with HR-positive, HER2-negative ABC at interim analysis: Significantly prolonged progression-free survival and improved response rates were demonstrated in the phase III, MONARCH 3 trial of abemaciclib in combination with the non-steroidal aromatase inhibitors (NSAI), anastrozole or letrozole, in patients with hormone receptor (HR)-positive, HER2-negative advanced breast cancer (ABC). (2360_PR - A. Di Leo, et al.)

Genomic landscape of patients with TNBC and disease recurrence investigated:

Patients experiencing disease progression after being treated with a neoadjuvant EGFR targeting agent plus chemotherapy for triple negative breast cancer (TNBC) showed distinctive genomic alterations rather than a comprehensive genomic pattern, according to findings from a

hypothesis-generating study. (LBA12 – Radosevic-Robin N, et al.)

Strong association exists between tumour type and survival in early breast cancer: The risk of death varies in patients diagnosed with early breast cancer depending upon the type of tumour they have, according to findings from an analysis of a large patient cohort in an ongoing study. (LBA15 – Cox D, et al.)

Ovarian cancer

September 8, 2017

Rucaparib shows clinical benefit as maintenance therapy in patients with recurrent ovarian cancer: Women with platinum-sensitive, recurrent, high-grade ovarian, fallopian tube, or primary peritoneal cancer who took the PARP inhibitor rucaparib as a maintenance therapy demonstrated improved progression-free survival compared to placebo in the randomised phase III ARIEL3 trial. (LBA40_PR – Ledermann J, et al.)

Patients with platinum sensitive ovarian cancer maintain QoL during maintenance niraparib therapy: Niraparib is a well-tolerated maintenance therapy that provides longer progression free-survival than placebo in patients with recurrent, platinum-sensitive ovarian cancer, who also maintain their quality of life (QoL) for the duration of niraparib maintenance. (930O - Oza AM, at al.)

September 9, 2017

Overall survival benefit is seen with olaparib in patients with ovarian cancer and TP53 disruptive mutation status: An analysis of data from a phase II trial comparing olaparib to placebo showed that olaparib yielded improved overall survival in all patients with mutated BRCA irrespective of the TP53 status and also in patients with BRCA wild-type in tandem with disruptive mutations in the TP53 DNA repair gene. (LBA42 – Martinez Bueno A, et al.)

Upper GI cancers

September 8, 2017

Pembrolizumab demonstrates antitumour activity in advanced gastric cancer as monotherapy and combined with chemotherapy: Pembrolizumab continues to demonstrate promising clinical activity in patients with advanced gastric or gastroesophageal junction cancer, according to updated findings from the KEYNOTE-059 study. (LBA28_PR – Wainberg ZA, et al.)

Gastrointestinal cancers

September 10, 2017

<u>Biomarker analysis reveals different genes are upregulated after lenvatinib and sorafenib</u> treatment in unresected HCC: Overall survival (OS) data and patient samples from a phase III trial comparing lenvatinib to sorafenib in patients with unresectable hepatocellular carcinoma (HCC) that were used to detect putative biomarkers for response to both agents revealed that VEGF- and FGF-family gene expression levels that were associated with greater OS. (LBA30 – Finn RS, et al.)

Location of the primary tumour, but not KRAS mutations, may indicate SIRT survival benefit in mCRC: Although the expected improvements in survival did not emerge from a large analysis of data comparing selective internal radiotherapy (SIRT) plus standard chemotherapy to chemotherapy in patients with metastatic colorectal cancer (mCRC) and inoperable liver metastasis, an unanticipated potential benefit was observed with SIRT in patients having primary tumours originating on the right side of the colon. (LBA26 – Wasan H, et al.)

Prostate cancer

September 8, 2017

Adding abiraterone acetate or docetaxel plus prednisone to standard of care in patients with high-risk prostate cancer: Patients with high-risk prostate cancer beginning long-term androgen deprivation therapy (ADT) showed similar outcomes from the addition of abiraterone acetate plus prednisolone or docetaxel plus prednisone, according to findings from the STAMPEDE trial. Both treatments have shown practice-changing benefits over the previous standard of care of first line ADT with further treatments on relapse. (LBA31_PR – Sydes MR, et al.)

Significant clinical activity demonstrated with 177Lu-PSMA617 in mCRPC:

Over half of the patients with progressive metastatic castrate-resistant prostate carcinoma (mCRPC) who progressed after standard therapies, achieved a greater than 50% reduction in PSA levels after receiving 177Lu-PSMA617. After receiving the first dose, many patients reported significantly improved quality of life including relief of bone pain. (7850 – Hofman MS, et al.)

Germline mutations in DNA repair genes lowers survival in mCRPC: Patients with metastatic castration resistant prostate cancer (mCRPC) and germline mutations in the BRCA1, BRCA2, ATM, or PALB2 genes tended to be younger and have non-statistically significant trends towards shorter cause-specific and progression-free survival compared to similar patients without mutations. Only patients with BRCA2 mutations showed significantly worse outcomes in planned subgroup analyses. (LBA32 – Castro Marcos E, et al.)

CNS malignancies

September 8, 2017

Combined nivolumab and radiotherapy ± temozolomide is safe in patients with newly diagnosed glioblastoma: A combination of the immunotherapeutic agent nivolumab plus standard radiotherapy with or without temozolomide is safe in patients with newly diagnosed glioblastoma, supporting further development for treatment of these patients, who currently have a poor prognosis and few treatment options. (3250 - Lim M, et al.)

<u>PD-L1 as a prognostic factor in patients with glioblastoma</u>: The intratumoural staining pattern of PD-L1 and the intensity of PD-1 staining in tumour infiltrating lymphocytes emerged as potentially positive prognostic factors in patients with glioblastoma, according to findings from a retrospective analysis. (326O - Şener Dede D, et al.)

Lung cancer

September 9, 2017

<u>Durvalumab as consolidation therapy prolongs PFS in stage III NSCLC patients without progression following platinum-based chemoradiotherapy</u>: Progression-free survival (PFS) was significantly improved with durvalumab when used as consolidation therapy in patients with locally-advanced, unresectable non–small-cell lung cancer (NSCLC) who had not progressed following standard care with platinum-based concurrent chemoradiotherapy, according to results from the phase III PACIFIC trial. (LBA1_PR - Paz-Ares L, et al.). Results have been simultaneously published in <u>The New England Journal of Medicine</u>.

Front-line osimertinib poised to become standard of care in EGFR-mutation positive NSCLC: First-line oral osimertinib significantly prolonged progression-free survival compared to the standard of care among patients with Ex19del/L858R EGFR mutated advanced non–small cell lung cancer (NSCLC), according to results from the phase III FLAURA study. (LBA2_PR - Ramalingam SS, et al.)

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<u>First-line dabrafenib and trametinib shows substantial clinical activity in BRAF V600E-mutated metastatic NSCLC</u>: Three-fourths of patients with previously untreated BRAF V600E-mutated non-small-cell lung cancer (NSCLC), receiving a combination of a BRAF inhibitor dabrafenib plus a MEK inhibitor trametinib, achieved complete or partial response or stable disease by investigator assessment and independent review, according to findings from a phase II trial. (LBA51 – Planchard D, et al.)

Basic science and translational research

September 9, 2017

Tumour subtype specific genetic alterations detected by comprehensive genomic profiling: Large scale comprehensive genomic profiling of more than 100,000 advanced cancers identified potentially actionable oncogenic rearrangements including kinase domain duplications and kinase fusions that may have therapeutic implications. (17000 – Gay LM, et al.)

Subtypes of thymic carcinomas show different genomic alterations and tumour mutational burden: Comprehensive genomic profiling may be used to identify genomic alterations in the highly variable histologic subtypes of thymic gland carcinoma that may also inform treatment decisions. (17010 – Ross JS, et al.)

<u>Large dataset of targetable genomic alterations created using liquid biopsy:</u> The investigators determined the somatic genomic profiles in 35,492 plasma samples that were obtained from 30,026 patients with advanced cancer using a cell free circulating tumour DNA next-generation sequencing test that targeted up to 73 genes. (17020 – Pal SK, et al.)

Palliative and supportive care

September 9, 2017

<u>Clinical trial toxicity reporting by investigators may not reflect patients' viewpoint</u>: An analysis comparing health related quality of life (HRQoL) by patient assessment and toxicity reporting by physicians in clinical trials demonstrated little agreement on many symptoms between the two, indicating that patients and investigators may not be on the same page regarding the overall patient clinical trial experience. (14220 – Brandberg Y, et al.)

<u>Sub-study of the GAND-emesis trial with neurokinin-1 receptor antagonist during concomitant chemoradiotherapy for cervical cancer</u>: Nausea had less of an impact on the daily function of women with cervical cancer treated with fosaprepitant in combination with palonosetron and dexamethasone during five weeks of chemoradiotherapy as compared to similar woman receiving placebo. (1540O – Ruhlmann CH, et al.)

Genitourinary malignancies

September 9, 2017

<u>Progression-free rate unaffected by sequence of cytoreductive nephrectomy and sunitinib in patients with synchronous mRCC</u>: Treating primary tumours by administering targeted therapy with sunitinib prior to cytoreductive nephrectomy (CN) did not improve the progression-free rate

at 28 weeks over a sequence of immediate CN followed by sunitinib in patients with synchronous metastatic renal cell carcinoma (mRCC). (LBA35 – Bex A, et al.)

September 10, 2017

Nivolumab plus ipilimumab versus sunitinib in first-line treatment for advanced or metastatic RCC: Combined immunotherapy with nivolumab plus ipilimumab resulted in a greater objective response rate and prolonged progression-free survival compared to sunitinib in intermediate-and poor-risk patients with previously untreated advanced or metastatic renal cell carcinoma (RCC), according to findings from the CheckMate-214 study. (LBA5 – Escudier B, et al.)

Ramucirumab improves PFS in patients with platinum refractory advanced urothelial carcinoma: Adding ramucirumab to docetaxel led to a statistically significant improvement in progression-free survival as compared to docetaxel plus placebo in patients with advanced or metastatic platinum refractory urothelial carcinoma, according to findings from the phase III RANGE trial. (LBA4 PR – Petrylak DP, et al.)

<u>Pembrolizumab continues to show greater benefit over chemotherapy in recurrent, advanced urothelial carcinoma</u>: The PD-L1 inhibitor pembrolizumab continued to demonstrate a survival benefit compared to chemotherapy among patients with advanced urothelial carcinoma, according to mature findings from the KEYNOTE-045 study. (LBA37_PR – de Wit R, et al.)

Sarcomas

September 9, 2017

<u>Promising results demonstrated with DCC-2618 in GIST</u>: Patients with gastrointestinal stromal tumours (GIST) showed promising responses to DCC-2618, a potent pan-KIT and PDGFRα kinase switch control inhibitor that has activity across a broad range of tyrosine kinase inhibitor treatment-emergent mutations. (14730 – Janku F, et al.)

Adjuvant imatinib recommended only for patients with high-risk GIST: Long-term results from a trial comparing adjuvant imatinib treatment to observation after R0/R1 surgery for gastrointestinal stromal tumour (GIST) support the recommendation to administer imatinib in this setting only in patients with high-risk GIST. (LBA55 – Casali PGG, et al.)

Haematological malignancies

September 10, 2017

Biosimilar rituximab shows equivalent efficacy to reference rituximab in previously untreated advanced follicular lymphoma: Treatment with GP2013-CVP met the primary endpoint of equivalence in overall response rate compared to rituximab-CVP in a confirmatory phase III ASSIST-FL trial that was conducted in patients with previously untreated, advanced-stage follicular lymphoma. (994O – Jurczak W, et al.)

Patients receiving radioactive iodine for well-differentiated thyroid cancer have an increased risk of AML: Acute myeloid leukaemia (AML) is more likely to occur in patients treated with surgery plus radioactive iodine (RAI) as opposed to patients receiving just surgery for well-differentiated thyroid cancer (WDTC). Furthermore, patients developing AML after successful RAI therapy for WDTC had a far poorer prognosis than patients treated for WDTC that did not develop AML, and also compared to patients with de novo AML, with no prior history of cancer or anti-cancer treatment. (9960 – Molenaar RJ, et al.)

Neuroendocrine tumours

September 10, 2017

<u>First KEYNOTE-028 report of pembrolizumab activity in patients with PD-L1-positive pNETs and carcinoid tumours</u>: Pembrolizumab provided objective response and stable disease in heavily pretreated patients with high grade pancreatic neuroendocrine tumours (pNETs) or carcinoid tumours demonstrating PD-L1 expression, according to data from carcinoid and pNET cohorts of the KEYNOTE-028 study. (4270 – Mehnert JM, et al.)

Immune landscape of PanNETs: Immune profiling of samples obtained from patients with pancreatic neuroendocrine tumours (PanNETs) identified a pattern of gene expression in the metastasis-like primary subtype of PanNETs that may inform the use of immunotherapy. (4280 – Young K, et al.)

Improved survival demonstrated with NSCLC-chemotherapy in pulmonary large cell neuroendocrine carcinoma with RB1 wild-type: Patients with specific genomic subtypes of pulmonary large cell neuroendocrine carcinoma (LCNEC) demonstrated significantly improved survival when treated with a chemotherapy regimen designed for non-small cell lung cancer over chemotherapy for small-cell lung cancer. (4310 – Derks J, et al.)

Melanoma

September 11, 2017

Adjuvant dabrafenib plus trametinib significantly lowers risk of death in stage III BRAF V600—mutated melanoma: Combined dabrafenib plus trametinib as an adjuvant treatment for patients with high-risk BRAF V600-mutated melanoma after surgical resection significantly decreased the risk of death or recurrent disease, according to findings from the phase III COMBI-AD study. (LBA6_PR – Hauschild A, et al.)

BRIM8 data shows benefit with adjuvant vemurafenib in resected BRAFV600 positive melanoma: Adjuvant vemurafenib provided substantial benefit to patients with completely resected stage IIC-IIIB BRAFV600 positive melanoma at high recurrence risk, where fewer disease-free survival events and distant metastasis-free survival events were observed with vemurafenib compared to placebo. (LBA7 PR – Lewis K, et al.)

Nivolumab bests ipilimumab as adjuvant therapy in resected melanoma: Patients with stage IIIb/IIIc or stage IV melanoma at high risk of recurrence following complete surgical resection had greater recurrence-free survival with adjuvant nivolumab compared to adjuvant ipilimumab, according to results from the phase III CheckMate 238 study. (LBA8_PR – Weber J, et al.)

AYA cancers

September 11, 2017

Video: Mapping the status and needs in AYA cancer care - ESMO/SIOPE European Landscape: The research findings highlight under-provision and inequity of adolescent and young adults (AYA) cancer care across Europe. Less than one third of European health-care providers who treat AYA with cancer have access to specialised centres, research initiatives and cancer services for late side effects management for this group of patients with special needs. Simultaneously published in the ESMO Open. (1438O_PR - Saloustros E, et al.)

Head and Neck cancer

September 11, 2017

<u>Durvalumab shows promising clinical benefit in recurrent/metastatic head and neck squamous cell carcinoma</u>: Patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) with high PD-L1 expression who have progressed on platinum-based chemotherapy mounted a strong response to the anti-PD-L1 immunotherapy durvalumab. (1042O – Zandberg D, et al.)

<u>Nivolumab demonstrates antitumour activity post-progression in recurrent/metastatic HNSCC</u>: Antitumour activity was observed when nivolumab was continued post-progression in patients

with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) who progressed on nivolumab after experiencing prior recurrence within 6 months of platinum-based chemotherapy. (1043O – Haddad R, et al.)

<u>Single agent atezolizumab in head and neck cancer</u>: Monotherapy with the checkpoint inhibitor atezolizumab demonstrated promising efficacy in patients with advanced head and neck cancer that was independent of both PD-L1 expression status on immune cells and the presence of human papilloma virus infection. (1044O – Bahleda R, et al.)

Cancer immunology and immunotherapy

September 11, 2017

Combined therapy with nivolumab and ISA 101 vaccine results in promising efficacy in HPV-positive oropharyngeal cancer: Treatment with the checkpoint inhibitor nivolumab combined with ISA 101, a synthetic long-peptide vaccine directed against human papilloma virus (HPV) 16 improved response in patients with incurable oropharyngeal cancer, compared to historical data with nivolumab alone. (11360 – Glisson B, et al.)

Rocapuldencel-T shows potential benefit in metastatic renal cell carcinoma: Promising clinical benefit was demonstrated in the trial of rocapuldencel-T plus standard-of-care therapy (SOC) versus SOC therapy alone in patients with newly diagnosed metastatic renal cell carcinoma. (11370 – Figlin R, et al.)