REPORT ESMO 2017 MADRID: RESPIRATORY ONCOLOGY

Els Wauters / Johan Vansteenkiste, Univ. Hospital KU Leuven and Leuven Lung Cancer Group

Full abstracts of this great ESMO in our field (3 respiratory abstracts in the presidential session) can be found at http://www.esmo.org/Conferences/ESMO-2017-Congress/Abstracts .

OUR 10 MESSAGE HIGHLIGHTS

Early stage NSCLC

1. ***#12730-PR: First randomized study comparing follow-up with chest X-ray (CXR) vs. CT scan for completely resected NSCLC (IFCT 0302).*** Large study (n=1,775), mainly consisting of stage I-II patients (82%). After a minimum follow-up of 4 years (median 8 yrs. 10 mo.), the primary endpoint of improved overall survival (OS) with CT-based follow-up was not met (HR 0.95). CT scan proved more sensitive in detecting early recurrences, however with no OS benefit. But, in patients that did not experience a recurrence/second primary at 24 mo. of follow-up, continued annual CT scan did significantly improve OS (P<0.05). Hence, based on the kinetics of recurrences after resection and given the higher sensitivity of CT scans to detect treatable recurrences/second primaries, the current ESMO guidelines can still be considered appropriate: i.e. surveillance every 6 months the first 2 years with a CT-scan at 12 and 24 months, followed by yearly surveillance with CT-scan.

Locally advanced NSCLC

2. ***#LBA1-PR: Durvalumab maintenance therapy vs. placebo in stage III unresectable NSCLC radically treated with chemoradiotherapy (PACIFIC).*** This planned interim analysis shows a highly significant benefit of 12 mo. adjuvant therapy with durvalumab, with a clinically relevant improvement in progression free survival (PFS) (16.8 vs. 5.6 mo., HR 0.52) and in time to death or distant metastasis (23.2 vs. 14.6 mo., HR 0.52). In addition, the safety profile was manageable. Mature OS data are awaited.

Advanced NSCLC targeted therapy

EGFR mut+ NSCLC:

3. ***#LBA2-PR: First-line Osimertinib vs. current standard of care EGFR-TKI in EGFR mut+ NSCLC (FLAURA).*** This study shows superiority of the 3rd generation EGFR-TKI Osimertinib with respect to PFS (18.9 vs. 10.2 mo., HR 0.46) and duration of response (17.2 mo. vs. 8.5 mo.). Safety profiles were largely comparable between both drugs, however with lower grade ≥3 adverse events (AEs) in the Osimertinib arm. These data open the possibility for frontline use of Osimertinib for EGFR mut+ NSCLC. However, final OS data of FLAURA and AURA3 are needed to decide on the optimal sequence of the different generation EGFR TKIs to ultimately improve OS.

ALK+ NSCLC:

4. ***#LBA50: Final OS analysis of Crizotinib vs. chemotherapy in treatment-naïve ALK mut+ NSCLC (PROFILE 1014).*** Long-term follow-up shows high 4-year OS rates in ALK+ NSCLC patients, and this in both treatment arms: 56.6% vs. 49.1%. OS was slightly in favor of Crizotinib, but the difference was not statistically significant: median not reached (NR) vs. 47.5 mo. (HR 0.76). This stresses the importance of subsequent treatments following progression in ALK+ NSCLC. Indeed, in the chemotherapy arm, 84% of patients received Crizotinib in second-line and 25% received another ALK TKI in further lines, contributing to the remarkable median OS. Overall, the data indicate that patients should always receive ALK TKI therapy, in a sequential manner, either preceded or followed by chemotherapy.
5. ***#2980-PR: Comprehensive data of central nervous system (CNS) activity of Alectinib vs. Crizotinib in treatment-naïve ALK+ NSCLC (ALEX).*** In patients with asymptomatic brain metastasis at

baseline, with or without prior brain radiotherapy, Alectinib significantly improved overall PFS vs. Crizotinib: NR vs. 12.7 mo. (HR 0.34) and 14.0 mo. vs. 7.2 mo. (HR 0.44), respectively. In addition, time to CNS progression was significantly longer in the Alectinib arm, both in patients with and without CNS disease at baseline (HR 0.18 and 0.14, respectively). These data further support the superior CNS activity of Alectinib compared to Crizotinib.

BRAF mut+ NSCLC:

6. ***#LBA51: First report of dabrafenib and trametinib for untreated BRAF V600E mut+ NSCLC (BRF113928):*** This 1st line cohort of the larger ph2 study confirms the efficacy of dabrafenib and trametinib in BRAF V600E mut+ NSCLC. In agreement with results in the relapse setting, ORR was 64% and median PFS was 10.9 mo. Toxicity should be taken into account, as nearly half of the patients experienced a serious, but manageable AE (grade ≥3, 69%). EMA has approved this combination for BRAF V600E mut+ advanced NSCLC (all lines). Consequently, screening for the presence of BRAF mutations should now be standard of care in newly diagnosed advanced NSCLC.

Advanced NSCLC immunotherapy

7. ***#12970: First prospective data of continuous nivolumab vs. stop after one year of treatment in previously treated advanced NSCLC (CM 153):*** Patients still on treatment after one year (only 220 out of 1,225, 18%) were randomly assigned to stop or to continue nivolumab. Continuation resulted in a significantly better median PFS: NR vs. 10.3 mo. from randomization (HR 0.42), both in CR/PR as well as SD at the time of randomization. There were more treatment-related AE in the continuation arm, but overall there were few new events after randomization. The optimal duration of immunotherapy, as well as the benefit of nivolumab retreatment after disease progression in patients that already stopped, should be determined in future prospective trials.
8. ***#12950: Tumor mutational burden in blood (bTMB) as a novel non-invasive predictive biomarker for response to atezolizumab in relapsed NSCLC (POPLAR/OAK):*** In agreement with tissue-based analysis, this study shows - for the first time in blood! - a positive correlation between TMB and clinical benefit of atezolizumab vs. docetaxel, both for PFS and OS. Interestingly, bTMB did not correlate with PD-L1 expression. Hence, bTMB may provide a novel non-invasive independent predictive biomarker for response to immunotherapy. Prospective studies are ongoing (BFAST).

Malignant pleural mesothelioma

9. ***#1618PD: First report of OS on chemotherapy±nintedanib in treatment-naïve MPM patients (LUME-Meso).*** The improvement in PFS with the addition of nintedanib to chemotherapy was confirmed (9.4 vs. 5.7 mo., HR 0.54), with the greatest benefit in the epithelioid subtype. OS data favor nintedanib (18.3 vs 14.2 mo., HR 0.77), however with a non-significant difference. AE were manageable and, importantly, the addition of nintedanib did not result in more frequent treatment discontinuation. At this moment, the confirmatory ph3 study results are awaited.
10. ***#LBA58: Update of Nivolumab or Nivolumab±Ipilimumab in relapsed MPM (IFCT 1501).*** Compared to the poor results of standard relapse chemotherapy (vinorelbine or gemcitabine) for MPM, this study shows a promising median OS of 13.6 mo. with nivolumab monotherapy, while median OS in the combination arm was not yet reached at time of data cut-off (median follow-up of 15 mo.). Toxicity is generally manageable, but of concern with combination therapy (5% grade 5 AEs). Results of randomized ph3 trials in MPM are awaited.

For your calendar: Respiratory Oncology Update 2017: 11 November, La Hulpe (https://www.update-respiratoryonco.be/en/Programme_20_818.html)