LSMO
Lebanese Society of Medical Oncology
الجمعية اللبنانية لأطباء الأورام الخبيث

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Cancer Immunotherapy Bulletin

Advances in the field of cancer immunotherapy have multiplied in the last years at an unprecedented pace and have changed the treatment paradigm in different types of cancer. Given the commitment of LSMO to medical education, we have issued this immuno-oncology newsletter to provide a brief update of the latest developments related to immunotherapy. In the digital era, this newsletter will be available on LSMO's updated website. The selection of the abstracts was done by the scientific committee of LSMO, with the support of Roche Lebanon.

We sincerely hope that the newsletter will add value to your clinical practice.

Nizar Bitar, MD
President of LSMO

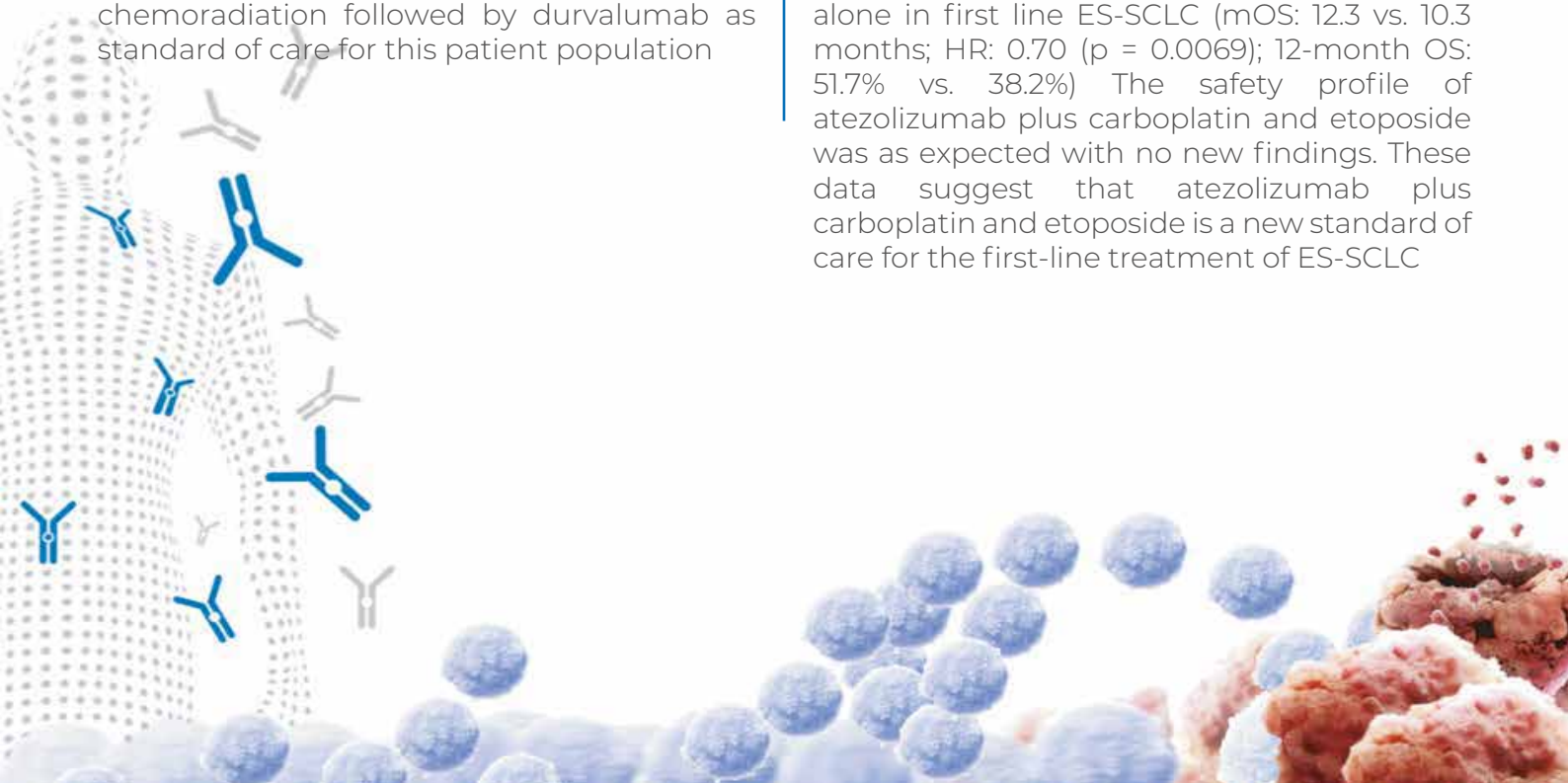
Fall 2018

Overall Survival with Durvalumab Versus Placebo After Chemoradiotherapy in Stage III NSCLC: Updated Results from PACIFIC (Antonia et al, WCLC 2018)

Locally advanced, unresectable, stage III NSCLC was typically treated with concurrent platinum-based chemotherapy and radiation. PACIFIC is an international, randomized, double-blind, placebo-controlled phase III trial of anti–PD-L1 mAb durvalumab in adults with unresectable stage III NSCLC and no disease progression after prior concurrent chemoradiation. This trial showed a survival advantage with durvalumab therapy HR: 0.68 (P = .0025). No new safety signals were identified. These data support concurrent chemoradiation followed by durvalumab as standard of care for this patient population

IMpower133: Primary PFS, OS and Safety in a PH1/3 study of first line Atezolizumab + Carboplatin + Etoposide in Extensive-Stage SCLC (Liu et al, WCLC 2018)

There has been little progress in the first line treatment of ES-SCLC in over 20 years. The majority of patients present with ES-SCLC and receive platinum (carboplatin or cisplatin) plus etoposide. IMpower133 evaluated the efficacy and safety of first line atezolizumab, a humanized monoclonal anti–PD-L1 antibody, or placebo, plus carboplatin and etoposide in ES-SCLC. The addition of atezolizumab to carboplatin and etoposide provided a significant improvement in OS and PFS, compared with carboplatin and etoposide alone in first line ES-SCLC (mOS: 12.3 vs. 10.3 months; HR: 0.70 (p = 0.0069); 12-month OS: 51.7% vs. 38.2%) The safety profile of atezolizumab plus carboplatin and etoposide was as expected with no new findings. These data suggest that atezolizumab plus carboplatin and etoposide is a new standard of care for the first-line treatment of ES-SCLC



IMpower132: efficacy of atezolizumab + carboplatin /cisplatin + pemetrexed as first line treatment in key subgroups with stage IV non-squamous non-small cell lung cancer (Papadimitrakopoulou et al, WCLC 2018)

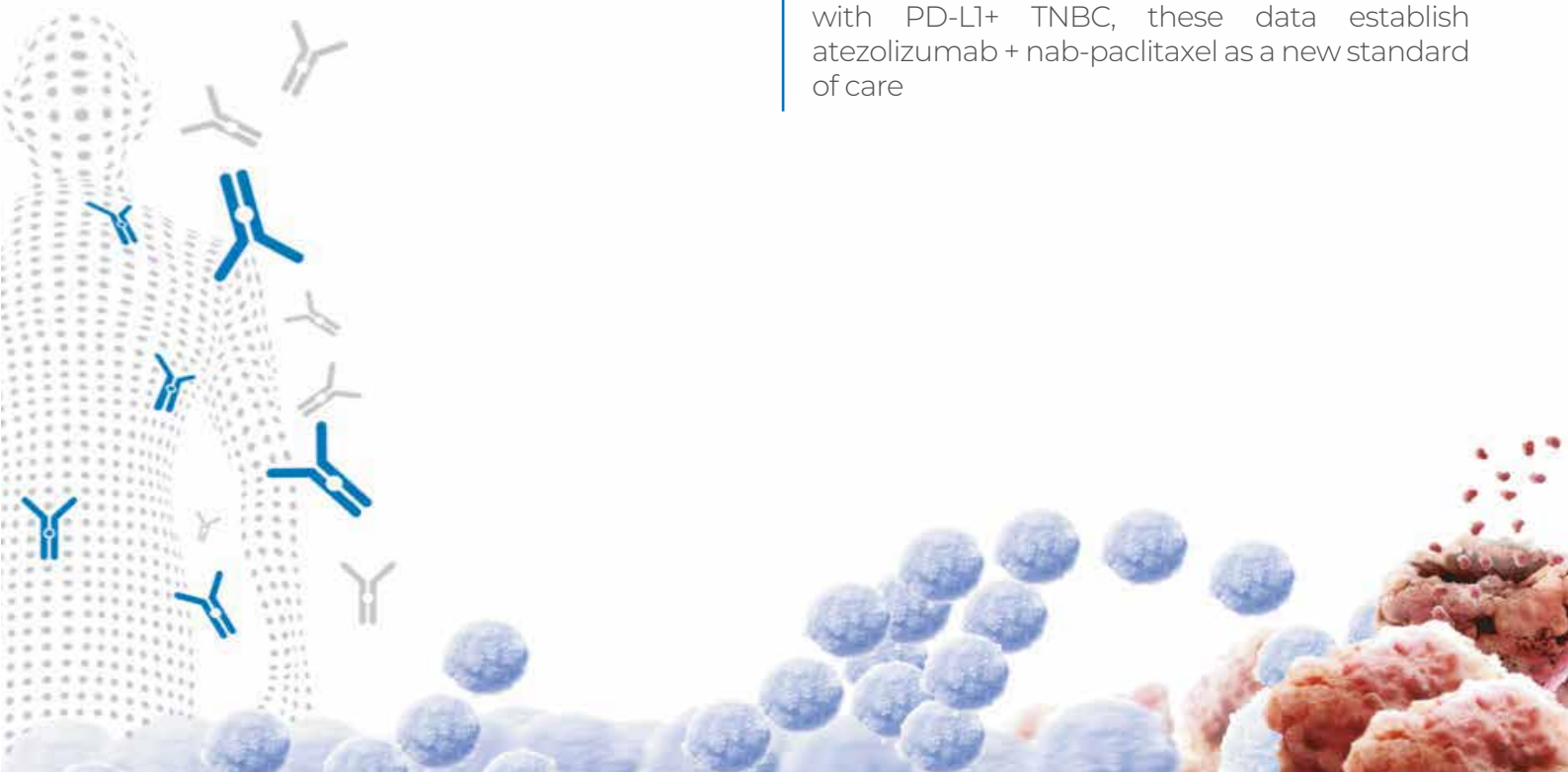
IMpower132 met its co-primary endpoint of investigator-assessed PFS in the ITT population. The addition of atezolizumab to carboplatin/cisplatin + pemetrexed improved median PFS in the ITT population (7.6 mo vs 5.2 mo, HR 0.60) and across key clinical subgroups. Atezolizumab + pemetrexed + carboplatin or cisplatin has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified. Final OS analysis is anticipated in 2019.

Avelumab vs Docetaxel for Previously Treated Advanced NSCLC: Primary Analysis of the Phase 3 JAVELIN Lung 200 Trial (Barlesi et al, WCLC 2018)

Avelumab, anti PDL1, showed increasing clinical activity in patients who had platinum-treated NSCLC with higher tumor PD-L1 expression. However, the trial did not meet its primary objective of improving OS vs docetaxel in PD-L1+ tumors (≥1% cutoff). OS findings may have been confounded by subsequent checkpoint inhibitor therapy in the docetaxel arm (5.7% vs 26.4%, in the avelumab and docetaxel arms respectively).

IMpassion130: Results from a global, randomised, double-blind, Phase III study of atezolizumab + nab-paclitaxel vs placebo + nab-paclitaxel in treatment-naive locally advanced or metastatic triple-negative breast cancer (Schmid et al, ESMO 2018)

IMpassion130 is the first Phase III study to demonstrate a benefit with first-line immunotherapy in mTNBC, a disease with high unmet medical need. Atezolizumab + nab-paclitaxel resulted in statistically significant PFS benefit in the ITT and PD-L1+ populations (ITT HR = 0.80 and PD-L1+ HR = 0.62). At this first interim OS analysis, a median OS improvement from 15.5 months to 25.0 months with atezolizumab + nab-paclitaxel in the PD-L1+ population, with a HR of 0.62 (formal OS testing in PD-L1+ patients not performed per hierarchical study design). Atezolizumab + nab-paclitaxel was well tolerated, with a safety profile consistent with each agent. For patients with PD-L1+ TNBC, these data establish atezolizumab + nab-paclitaxel as a new standard of care



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KEYNOTE-057: pembrolizumab in high-risk NMIBC unresponsive to BCG (De Wit et al, ESMO 2018)

Pembrolizumab demonstrated encouraging antitumor activity, with a compelling complete response rate and duration of response in patients with BCG-unresponsive carcinoma in situ (with or without papillary disease) who refused or were ineligible for cystectomy and who had limited alternative treatment options. These data are the first results from the phase II KEYNOTE-057 to be reported and the first report evaluating the efficacy of PD-L1/PD-1 inhibitors in BCG-refractory high-risk NMIBC.

Nivolumab alone or in combination with ipilimumab in patients with platinum-pretreated metastatic urothelial carcinoma, including the nivolumab 1 mg/kg + ipilimumab 3 mg/kg expansion from CheckMate032 (Rosenberg et al, ESMO 2018)

With extended follow-up, NIVO3, NIVO3+IPI1, and NIVO1+IPI3 regimens demonstrated sustained efficacy in patients with previously treated mUC. A trend toward higher ORR and longer median PFS and OS compared with previous reports of PD-1/PD-L1 monotherapies was observed with NIVO1+IPI3 in this PD-L1 unselected patient population, most of whom had received ≥2 chemotherapy regimens.

Javelin Renal 101: avelumab+ axitinib in RCC (Motzer et al, ESMO 2018)

JAVELIN Renal 101 is the first positive phase 3 study combining an immune checkpoint blocker avelumab with a tyrosine kinase inhibitor, axitinib compared to TKI alone in the first line treatment of advanced RCC. The combination benefit was shown in all subgroups of patients, by independent review as well as by investigators, and whether tumour cells stained positive for PD-L1 or not (mPFS 13.8 vs 8.4 months, HR = 0.69; P = .0001, irrespective of PDL1). The findings support the potential of avelumab plus axitinib as a new treatment approach for patients with advanced RCC.

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