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

SUMMER 2018

Pembrolizumab versus platinum-based chemotherapy as first-line therapy for advanced/metastatic NSCLC with a PD-L1 tumor proportion score (TPS) ≥ 1%: Open-label, phase 3 KEYNOTE-042 study. (Lopes et al, ASCO 2018)

KEYNOTE-042 is the first study with a primary end-point of OS to demonstrate superiority of pembrolizumab over platinum-based chemotherapy in patients with previously untreated advanced/metastatic NSCLC without sensitizing EGFR or ALK alterations and a PD-L1 tumour proportion score ≥1%. Pembrolizumab significantly improved OS in patients with TPS ≥50% (HR 0.69), TPS ≥20% (HR 0.77), and TPS ≥1% (HR 0.81). These data potentially extend the role of pembrolizumab monotherapy in the first line setting of metastatic NSCLC.

KEYNOTE 407 Phase 3 study of carboplatin-paclitaxel/nab-paclitaxel with or without pembrolizumab for patients with metastatic squamous non-small cell lung cancer (NSCLC). (Paz-Ares et al, ASCO 2018)

Adding pembrolizumab to chemotherapy significantly increased OS, PFS and almost doubled the ORR of chemotherapy for patients with untreated metastatic squamous NSCLC (58.4% compared to 35.0%, p-value 0.0004). Duration of response ≥6m was 65.8% for pembrolizumab+ chemotherapy and 45.6% for chemotherapy. Pembrolizumab+ chemotherapy elicited a tolerable safety profile. These data suggest this combination could become a new standard of care in first line metastatic squamous NSCLC.

Impower 150 Overall Survival Analysis of a Randomized Phase III Study of Atezolizumab + Chemotherapy ± Bevacizumab vs Chemotherapy + Bevacizumab in 1L Nonsquamous NSCLC (Socinski et al, ASCO 2018)

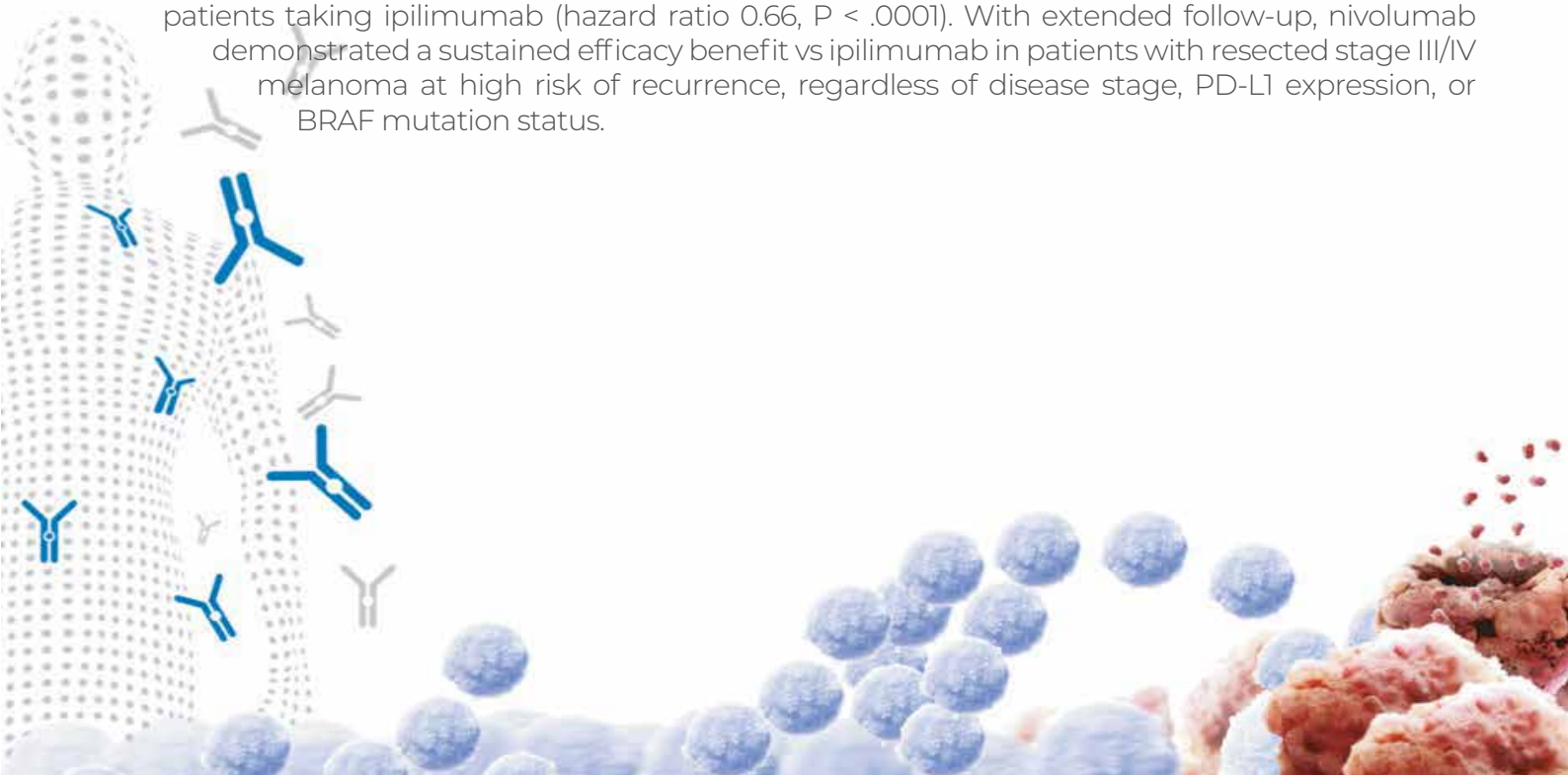
IMpower150 met its co-primary PFS and OS endpoints and demonstrated a statistically significant and clinically meaningful benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy in 1L nonsquamous NSCLC, across all PD-L1 subgroups. No new safety signals were seen. OS was improved for atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy (HR, 0.78; P = 0.016) in the ITT-WT. Populations of interest included patients with EGFR/ALK mutations previously treated with targeted therapies, and patients with liver metastases (HR=0.54), with clinical benefit shown with the addition of bevacizumab to atezolizumab + chemotherapy.

CM-227: P3 study of Nivolumab + Platinum-based chemotherapy vs. chemotherapy as 1L treatment for NSCLC with TPS <1% PD-L1 expression (H. Borghaei, ASCO 2018)

CheckMate 227, a phase 3 study of 1L nivolumab + ipilimumab , nivolumab, or nivolumab + chemotherapy vs chemotherapy in advanced NSCLC, met its co-primary endpoint of prolonged progression-free survival (PFS) with nivolumab + ipi vs chemotherapy in patients with tumor mutational burden ≥10 mutations/Mb. Results for nivolumab + chemotherapy vs chemotherapy in patients with < 1% tumor PD-L1 expression were reported. PFS was improved with nivolumab + chemotherapy vs chemotherapy (HR = 0.74). 1L nivolumab + chemotherapy improved PFS vs chemotherapy in patients with advanced NSCLC and < 1% tumor PD-L1 expression, and was well tolerated. CheckMate 227 Part 2 (ongoing) is evaluating nivolumab + chemotherapy vs chemotherapy irrespective of PD-L1 expression and will further inform benefit from this combination across different subgroups of NSCLC

Updated CM-238 results: P3 study of adjuvant nivolumab vs. ipilimumab after complete resection in stage III/IV Mel (Weber, ASCO 2018)

Patients with resected stage III/IV melanoma had better outcomes in terms of relapse-free survival (RFS) and distant metastases-free survival (DMFS) when treated with nivolumab versus ipilimumab. In the 24-month follow-up patients taking nivolumab continued to have a significantly longer RFS than patients taking ipilimumab (hazard ratio 0.66, P < .0001). With extended follow-up, nivolumab demonstrated a sustained efficacy benefit vs ipilimumab in patients with resected stage III/IV melanoma at high risk of recurrence, regardless of disease stage, PD-L1 expression, or BRAF mutation status.



Pembrolizumab monotherapy as 1L therapy in advanced clear cell RCC: Results from cohort A of KEYNOTE-427 (D.F. McDermott, ASCO 2018)

Programmed death-1 (PD-1) inhibitor–based combination therapy shows clinical benefit in first-line accRCC. However, data are limited on clinical impact of first-line PD-1 inhibitor monotherapy. KEYNOTE-427 is a single-arm, open-label, 2-cohort, phase 2 study that evaluates efficacy and safety of the PD-1 inhibitor pembrolizumab as first-line monotherapy in accRCC and anccRCC. Confirmed ORR by ICR was 33.6% . Median duration of response was not reached. Pembrolizumab monotherapy demonstrated promising efficacy and acceptable tolerability in patients with accRCC.

IMMotion 151 Randomized Phase III Study of Atezolizumab Plus Bevacizumab vs Sunitinib in Untreated Metastatic Renal Cell Carcinoma (mRCC) (Motzer, ASCO 2018)

This study investigated the addition of anti-VEGF and anti-PDL1 therapies. This phase III trial of a PD-L1/PD-1 pathway inhibitor combined with an anti-VEGF agent in 1L mRCC showed PFS HR for atezolizumab + bevacizumab vs sunitinib was 0.74 (95% CI 0.57, 0.96) in PD-L1+ patients and 0.83 (95% CI 0.70, 0.97) in ITT patients. Safety was consistent with that of the individual agents. These results support the use of atezolizumab + bevacizumab as a 1L treatment option in mRCC

CheckMate 214: nivolumab + ipilimumab vs sunitinib in 1L mRCC (quality of life) (Cella et al, ASCO 2018)

In CheckMate 214, overall survival (OS) with nivolumab + ipilimumab (N+I) was superior to sunitinib (S; HR, 0.63; P<0.001) with a manageable safety profile as first-line treatment for intermediate/poor (I/P)-risk patients with advanced renal cell carcinoma (aRCC). This is the first study to demonstrate a statistically significant overall survival benefit over sunitinib. Exploratory HRQoL analyses were conducted on RCC-specific symptoms from the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FKSI-19) and general cancer symptoms were assessed using the Functional Assessment of Cancer Therapy-General (FACT-G) instruments. In addition to the OS benefit and superior safety profile, descriptive data suggest that N+I offers significant and sustained HRQoL improvement vs S in I/P-risk patients with untreated aRCC

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Safety and Clinical Activity of Atezolizumab + Bevacizumab in a Phase Ib Study in First-Line Hepatocellular Carcinoma (Stein et al, ASCO 2018)

Advanced HCC is a lethal cancer with a high unmet medical need. Single-agent immunotherapy with PD-L1/PD-1 blockade or treatment with anti-angiogenic bevacizumab (anti-VEGF) has shown modest activity in HCC. The confirmed response rate of 62% suggests that atezo + bev in combination has synergistic clinical activity. The combination of atezo + bev is safe and well tolerated; no new safety signals were identified beyond the established safety profile for each agent. Expansion of this HCC cohort and evaluation of atezolizumab+bevacizumab in a Phase III study are under way.

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