1134P - Monalizumab in combination with cetuximab in patients (pts) with recurrent or metastatic (R/M) head and neck cancer (SCCHN) previously treated or not with PD-(L)1 inhibitors (IO): 1-year survival data (ID 1242)

Presentation Number
1134P
Lecture Time
12:00 - 12:00
Speakers

- Roger B. Cohen (Philadelphia, PA, United States of America)

30.09.2019
12:00 - 13:00

Abstract

Background

Monalizumab is a first in class immune checkpoint inhibitor targeting Natural Killer Group 2A (NKG2A), which is expressed as a heterodimer with CD94 on subsets of Natural Killer (NK), γδ T and tumor-infiltrating $CD8^+$ T cells (André et al. Cell 2018). The NKG2A ligand, HLA-E, is upregulated in cancer, including SCCHN. NKG2A blockade promotes innate anti-tumor immunity mediated by NK and $CD8^+$ T cells and enhances human NK cell antibody-dependent cell-mediated cytotoxicity (ADCC) induced by cetuximab. This dual targeting could provide greater antitumor activity than cetuximab alone.

Methods

The multicenter phase II trial tested the combination of monalizumab and cetuximab in pts with R/M SCCHN. Pts received monalizumab 10 mg/kg q2weeks and cetuximab according to the label until disease progression or unacceptable toxicity. Pts were required to be progressing after platinum-based chemotherapy and to have received ≤2 prior lines of therapy in the R/M setting. Previous treatment with IO was allowed. The primary endpoint was Overall Response Rate (ORR) per RECIST.

Results

All 40 pts received prior platinum-based chemotherapy, 18 (45%) prior IO and 5 (13%) prior cetuximab. ORR was 27.5% [95% confidence interval: 16-43] with 11 confirmed responses (1 complete + 10 partial) observed in both IO naive 36% [20-57] and IO pretreated pts 17% [6-39]. As of April 17, 2019, with a median follow-up of 17 months (mo), in all pts, IO naïve and IO pretreated pts respectively, median duration of response was 5.6, 5.3 and 5.6 mo, PFS was 4.5, 3.9 and 5.1 mo and OS was 8.3, 7.8 and 12.8 mo. The 12 mo OS estimate is 44% [31-63]. No new safety signal emerged. Pre and post treatment tumor biopsies were collected and RNA seq analyses are ongoing.

Conclusions

In a cohort of 40 patients of heavily pretreated SCCHN patients, monalizumab and cetuximab combination demonstrated high response rate, good duration of response, and promising PFS and OS as well as good safety profile. An additional R/M SCCHN cohort of 40 patients who received both platinum-based chemotherapy and IO is being enrolled in this study.

Clinical trial identification - NCT02643550.

1203P - Preliminary results of STELLAR-001, a dose escalation phase I study of the anti-C5aR, IPH5401, in combination with durvalumab in advanced solid tumours (ID 1285)

Presentation Number
1203P
Speakers

- Christophe Massard (Villejuif, CEDEX, France)

Date
30.09.2019
12:00 - 13:00

Abstract

Background

Anaphylatoxin C5a is released in the cancer microenvironment and binds to the C5aR receptor, which in turns promotes protumoral inflammation and immune suppression through recruitment and activation of myeloid derived suppressor cells (MDSC) and neutrophils. Overexpression of C5aR has been reported in several tumor types and correlates with aggressive tumor features and poor prognosis. Additionally, C5aR was found to be upregulated in NSCLC patients in progression after an initial response to an anti-PD-(L)1 therapy (aPD1). IPH5401, a fully human anti-C5aR1 antibody, inhibits the C5a mediated effects on MDSC and neutrophils. Preclinical data suggest that the combined blockade of C5aR1 and aPD1 synergistically reduce tumor growth and delay tumor progression. These data suggest that combining IPH5401 with aPD1 may improve efficacy and overcome secondary resistance to aPD1.

Methods

This is an ongoing phase I to evaluate the safety of IPH5401 + durvalumab (durva) in advanced solid tumors. In the 3 + 3 dose-escalation, patients (pts) receive IPH5401 at 4 dose levels (DL) (DL1, DL2, DL3 [Q1w] and DL4 [Q2w]) single agent during the first 2 weeks (w) then in combination with durva 1500 mg Q4w. Blood samples are collected at various time points for characterization of pharmacokinetics, pharmacodynamics and immunogenicity. Upon completion of the phase I part and determination of a recommended phase II dose, expansion cohorts in NSCLC and HCC will be activated.

Results

As of April, 30th 2019, 12 pts have been enrolled (4 HCC, 2 UCC, 5 NSCLC, 1 RCC). No DLT was seen to date. DL3 and DL4 are ongoing. A total of 11 treatment related AEs (TRAEs) were reported in 5 patients: G2 diarrhea with lymphocytic colitis (n = 1), G1 diarrhea (n = 1), G1 skin rashes (n = 2), G1 White blood cell decrease (n = 1), G1 pneumopathy (n = 1), G1 lung disorder (n = 1), G1 fatigue (n = 1), G1 arthralgia (n = 1), G1 back pain (n = 1), G1 musculoskeletal chest pain (n = 1). There were no grade 3/4 TRAEs and no TRAEs that led to study discontinuation.

Conclusions

Preliminary results of this combination of IPH5401 plus durva suggest a manageable toxicity profile. Results of dose escalation including PK/PD data will be presented.

Clinical trial identification - NCT03665129.

1201P - Durvalumab + monalizumab, mFOLFOX6, and bevacizumab in patients (pts) with metastatic microsatellite-stable colorectal cancer (MSS-CRC) (ID 3681)

Presentation Number
1201P
Lecture Time
12:00 - 12:00
Speakers

- May Cho (Sacramento, CA, United States of America)

30.09.2019
12:00 - 13:00

Abstract

Background

Immune checkpoint inhibitors have shown limited clinical benefits in MSS-CRC; dual targeting of non-redundant pathways may enhance antitumor immune response. In a phase I/II, multicenter, open-label study, the anti-PD-L1 antibody durvalumab (D) was combined with monalizumab (M), an IgG4 mAb that blocks NKG2A binding to HLA-E to reduce inhibition of NK and CD8+ T cells. The combination (D+M) was well tolerated and showed encouraging activity in heavily pretreated pts with advanced MSS-CRC. In a dose-exploration cohort, D+M was assessed in combination with standard of care (SOC) chemotherapy and bevacizumab, an anti-VEGF agent, as first-line therapy for advanced/metastatic MSS-CRC.

Methods

Eligible pts had histologically defined MSS-CRC, regardless of RAS/RAF mutational status, ECOG 0–1 and no prior systemic therapy. They received durvalumab 1500 mg Q4W, monalizumab 750 mg Q2W, modified FOLFOX6 (folinic acid, fluorouracil, and oxaliplatin) Q2W and bevacizumab 5 mg/kg Q2W until end of treatment; dose modifications were allowed according to SOC practice except during the DLT evaluation period. The primary endpoint was safety and tolerability of D+M with FOLFOX6 and bevacizumab; secondary endpoints included antitumor activity.

Results

As of Mar 25, 2019, 18 pts were enrolled with median follow-up of 6.2 months. Monalizumab-related adverse events (AEs) occurred in 13 (72%), serious in 1 (6%; embolism). Durvalumab-related AEs occurred in 14 (78%; none serious). All pts had chemotherapy-related AEs, serious in 1 (6%; febrile neutropenia) and 10 (56%) had bevacizumab-related AEs, serious in 2 (11%; embolism and febrile neutropenia). There were no grade 5 or dose-limiting toxicities. At 16 weeks, 17 pts were evaluable for response; 9 (53%) had partial responses (7 confirmed, 2 unconfirmed), 6 (35%) had stable disease and 2 (12%) had progressive disease; there were no complete responses. Median time to response for the 7 confirmed responders was 15.4 weeks; median duration of response was not yet reached.

Conclusions

First-line D+M combined with SOC showed manageable safety and preliminary activity in pts with advanced/metastatic MSS-CRC. Accrual is complete.

Clinical trial identification - NCT02671435