LBA15  Preliminary results of the first-in-human (FIH) study of MK-1454, an agonist of stimulator of interferon genes (STING), as monotherapy or in combination with pembrolizumab (pembro) in patients with advanced solid tumors or lymphomas


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Background: The STING pathway has been implicated in antitumor immunity and response to immune checkpoint inhibitors. Intratumoral (IT) administration of MK-1454, a cyclic dinucleotide STING agonist, results in complete tumor regression and enhances the efficacy of anti-PD1 therapy in mouse syngeneic models. Initial results of the MK-1454 FIH study as monotherapy (Arm 1) or in combination with pembro (Arm 2) in pts with solid tumors or lymphomas are presented.

Methods: A phase 1, open label, multicenter, dose escalation study. Eligible pts had a confirmed advanced solid tumor or lymphoma. MK-4621 was administered twice a week over a 4-week period. Dose escalation followed a 3 + 3 design to determine maximum tolerated dose or maximum feasible dose. Dose levels included pyrexia, chills, fatigue, injection site pain, and nausea (Arm 1) and pruritus (Arm 2). In both arms, dose dependent increases in systemic MK-1454 exposure (t1/2 >1.5 hr) and elevations in serum cytokines IL-6 and IP-10 and STING induced gene expression in blood were observed. Of 25 pts (first dosed by May 01, 2018) in Arm 2, 6 (24%) PRs were seen (3 HNSCC, 1 TNBC, 2 anaplastic thyroid carcinoma) with reductions in both target-injected and -noninjected lesions (median -83%); no CR/PR in Arm 1.

Results: As of Jul 31, 2018, 26 pts in Arm 1 and 34 in Arm 2 were treated. DLTs at 1500 ug were vomiting (1 pt, Arm 1) and injection site reactions (2 pts, Arm 2). An MTD has not been determined; dose escalation is ongoing. Treatment related adverse events (TRAEs) occurred in 83% and 82% of pts in Arms 1 and 2, 9% and 14% were grade ≥3 AEs, and resulted in discontinuation of 7% of pts in Arm 2 (0% in Arm 1); no deaths due to TRAEs occurred. Most common TRAEs in ≥10% of pts in Arms 1 and 2 included pyrexia, chills, fatigue, injection site pain, and nausea (Arm 1) and pruritus (Arm 2). In both arms, dose dependent increases in systemic MK-1454 exposure (t1/2 >1.5 hr) and elevations in serum cytokines IL-6 and IP-10 and STING induced gene expression in blood were observed. Of 25 pts (first dosed by May 01, 2018) in Arm 2, 6 (24%) PRs were seen (3 HNSCC, 1 TNBC, 2 anaplastic thyroid carcinoma) with reductions in both target-injected and -noninjected lesions (median -83%); no CR/PR in Arm 1 were observed. DCR was 20% (Arm 1) and 48% (Arm 2).

Conclusions: Combined MK-1454 plus pembro resulted in encouraging efficacy and an acceptable safety profile supporting continued development of the combination regimen.


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