

Encore from ESMO Virtual Congress 2020:

CheckMate 73L: A phase III study comparing nivolumab (NIVO) plus concurrent chemoradiotherapy (cCRT) followed by NIVO ± ipilimumab (IPI) versus cCRT followed by durvalumab (DURV) for previously untreated, locally advanced (LA) stage III non-small cell lung cancer (NSCLC).

**CheckMate 73L: A phase 3 study comparing nivolumab (NIVO) plus concurrent chemoradiotherapy (cCRT) followed by NIVO ± ipilimumab (IPI) versus cCRT followed by durvalumab (DURV) for previously untreated, locally advanced (LA) stage III non-small cell lung cancer (NSCLC)**

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## **ABSTRACT**

**Background:** Historically, the standard-of-care for patients with unresectable stage III NSCLC was cCRT; however, outcomes are poor with 5-y survival rates of 15–30%. While cCRT primes anti-tumour immunity, it also upregulates PD-L1 expression, potentially blunting any immune response. Thus, concurrent immunotherapy + cCRT may improve outcomes. The safety and tolerability of NIVO, an anti-PD-1 antibody, given concomitantly with cCRT in patients with stage III NSCLC was demonstrated in the phase 2 NICOLAS study (NCT02434081). Furthermore, combining NIVO with IPI, an anti-CTLA-4 antibody, resulted in a longer median overall survival (OS) versus chemotherapy in patients with advanced NSCLC who had PD-L1≥1% in the phase 3 CheckMate 227 study (NCT02477826). In a prespecified exploratory analysis, NIVO + IPI showed an efficacy benefit versus

NIVO. Previously, DURV, an anti-PD-L1 antibody, demonstrated significant improvements versus placebo in progression-free survival (PFS) and OS with manageable safety in patients without disease progression after cCRT in the phase 3 PACIFIC study (NCT02125461). Therefore, we will evaluate the efficacy of NIVO + cCRT followed by NIVO ± IPI versus cCRT followed by DURV for untreated, LA stage III NSCLC in the phase 3 randomized CheckMate 73L study (NCT04026412).

**Design:** In all, 888 patients aged ≥18 y with previously untreated stage III NSCLC and an ECOG PS ≤1 will be stratified by age, PD-L1 expression, and disease stage, then randomized (1:1:1) to receive NIVO (360 mg Q3W) + cCRT followed by NIVO (360 mg Q3W) + IPI (1 mg/kg Q6W; Arm A) or NIVO alone (480 mg Q4W; Arm B) for ≤1 y, or cCRT followed by DURV (10 mg/kg Q2W; Arm C) for ≤1 y. Patients with PD during cCRT will discontinue treatment and enter follow-up. Primary endpoints are PFS by RECIST 1.1, assessed by BICR (Arm AvsC) and OS (Arm AvsC). Secondary endpoints are PFS (Arm BvsA or C), OS (Arm BvsA or C), objective response rate, time to response, duration of response, time to distant metastases, and safety. Start date: Aug 2019.

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