ESMO virtual congress 2020—highlights NSCLC

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Summary This year's virtual version of the European Society for Medical Oncology (ESMO) presidential sessions included three “late breaking” non-small cell lung cancer (NSCLC) abstracts, discussing strategies for adjuvant therapy of localized disease and up-front treatment of advanced anaplastic lymphoma kinase (ALK)-positive lung cancer.

Keywords Non-small cell lung cancer · Tyrosine kinase inhibitors · Osimertinib · Lorlatinib · Adjuvant radiotherapy

CNS efficacy of adjuvant osimertinib Previously at ASCO 2020, three years of tyrosine kinase inhibitor (TKI) osimertinib were shown to improve disease-free survival (DFS) compared to placebo in stage IB–IIIA NSCLC with activating epidermal growth factor receptor (EGFR) mutations following standard surgery and adjuvant therapy [1]. Late breaking abstract No. 1 discussed further supportive data for this strategy, with a focus on the central nervous system (CNS) activity of this treatment concept [2]. CNS efficacy was evaluated in terms of CNS-DFS as a predefined exploratory endpoint of the phase III trial ADAURA. Remarkably, adjuvant osimertinib resulted in an 82% risk reduction of CNS relapses (HR 0.18, 95% confidence interval [CI] 0.10–0.33, $p < 0.0001$). At the presented data cut-off, a CNS relapse was documented in 1% (4/339) of patients in the osimertinib arm versus 10% (33/343) in the placebo cohort. The corresponding CNS-DFS rate at 36 months was improved with 98% versus 82%. *Key message:* These data confirm once

more the CNS efficacy of osimertinib for EGFR-positive patients and osimertinib was recently approved by the US Food and Drug Administration for the adjuvant therapy of NSCLC patients with EGFR exon 19 deletion or exon 21 L858R mutations.

Postoperative radiotherapy for N2 disease A further clinically highly relevant study for localized NSCLC investigated the role of adjuvant postoperative radiotherapy (PORT) in N2 disease, a widely performed practice but also matter of debate due to lack of systematic data. LungART, a European randomized phase III study, was the first randomized study to address this question [3]. A total of 501 patients with NSCLC stage III N2 disease were randomized either to PORT with 54 Gy in 27–30 fractions or observation-only. Prior (neo-)adjuvant chemotherapy was allowed. PORT resulted in a nonsignificant improvement of DFS, with 30.5 months for the intervention group versus 22.8 months in the control arm (hazard ratio [HR] 0.85, 95% CI 0.67–1.07, $p = 0.16$). Overall-survival (OS) at 3 years was comparable at 66.5% for PORT versus 63.8% without. As expected, the mediastinal recurrence rate was reduced by 50% following PORT but there was a higher rate of deaths reported as censoring events in the intervention group (14.6% of all DFS events versus 5.3%). Furthermore, the rate of cardiotoxicity was increased in the radiotherapy group. One caveat, however, is the long recruitment period of more than 10 years, which potentially raises technical discussions. *Key message:* The presented results of the LungART study discourage use of PORT for N2 patients on a routine basis.

Upfront treatment with lorlatinib in advanced ALK-positive NSCLC The third late breaking abstract presented data on the first line use of anaplastic lymphoma kinase (ALK) inhibitor lorlatinib for ad-

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vanced ALK-positive NSCLC [4]. The randomized open label phase III study CRWON evaluated the efficacy of lorlatinib versus crizotinib in this setting. A planned interim analysis of the primary endpoint progression-free survival (PFS) was presented. Lorlatinib significantly prolonged median PFS versus crizotinib in previously untreated patients (median PFS not reached versus 9.3 months, HR 0.28, 95%CI 0.19–0.41). The 1-year PFS was clinically relevantly increased with 78% versus 39%. The observed PFS benefit was persistent across subgroups including the cohort of patients with brain metastases. Grade III and IV toxicity was slightly elevated but included mostly laboratory findings such as lipid abnormalities. Patient-reported outcomes showed improvement in quality of life for lorlatinib versus crizotinib ($p < 0.01$). **Key message:** These results suggest a high activity of lorlatinib front-line; longer follow-up data and comparison with further next generation ALK inhibitors will be important for the definitive positioning of this TKI.

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Conflict of interest B. Kiesewetter declares that she has no competing interests.

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