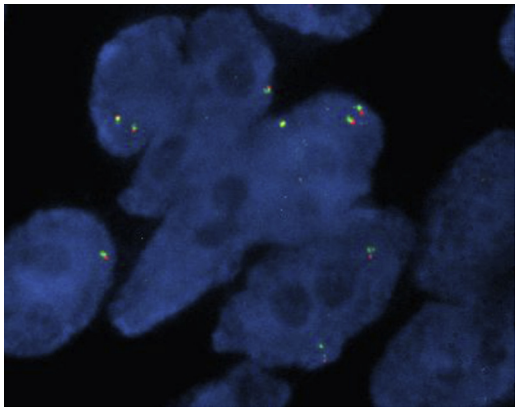
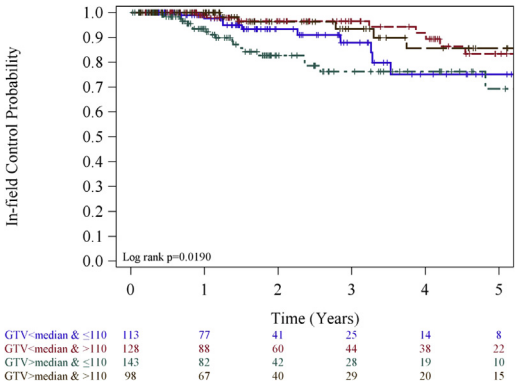
In This Issue

Comparison of Molecular Testing Modalities for Detection of *ROS1* Rearrangements in a Cohort of Positive Patient Samples



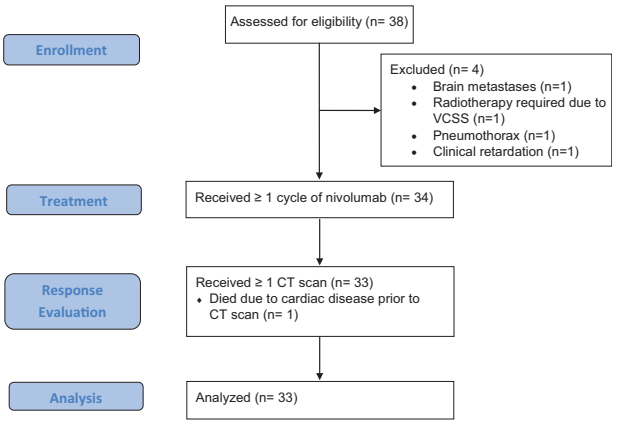
Three common molecular testing approaches were compared for the performance in detecting *ROS1* rearrangements in 23 clinical samples positive for *ROS1* abnormalities. These testing methods were break-apart fluorescence in situ hybridization (FISH), DNA-based hybrid capture library preparation followed by next-generation sequencing (NGS), and RNA-based anchored multiplex polymerase chain reaction library preparation followed by NGS. The analysis demonstrated that none of the methods showed 100% sensitivity in *ROS1* detection. Negative results were observed in 2 of 20 samples with FISH, 4 of 18 with DNA-based NGS assay, and 3 of 19 in RNA-based NGS assay. Potential characteristics of the 3 assays analyzed that led to false-negative results were identified. Genomic breakpoints were determined to be an unreliable predictor of breakpoints at the transcript level possibly as a result of alternative splicing. In summary, the findings suggest that the molecular testing methods have limitations in detecting *ROS1* rearrangement/fusion in the complex clinical settings, warranting careful result interpretations. (p. 1474)

Histology, Tumor Volume, and Radiation Dose Predict Outcomes in NSCLC Patients After Stereotactic Ablative Radiotherapy



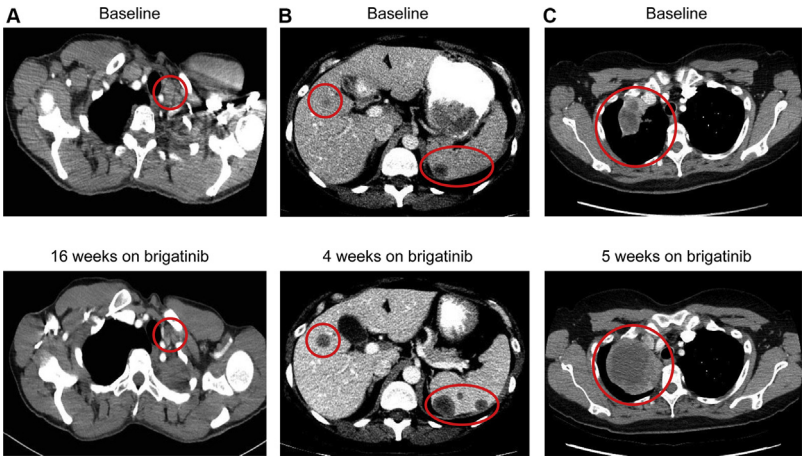
Characteristics associated with outcomes from stereotactic ablative body radiotherapy were evaluated in a cohort of early-stage NSCLC patients treated with 3-5 fractions, with complete dosimetric information in 442 patients with 482 lesions out of 508 patients with 561 lesions. The follow-up at median 6.7 years showed the rates of a 3-year in-field control at 88.1%, involved lobe control at 80.0%, overall survival at 49.4%, and progression-free survival at 37.2%. Gross tumor volume (GTV) (hazard ratio [HR] = 1.01 per mL; $p = 0.0044$) and histology ($p = 0.0225$) were independently associated with involved lobe failure. In-field failure was associated independently with GTV (HR = 1.013; $p = 0.001$) and GTV dose (cutoff of 110 Gy, biologically effective dose with $\alpha/\beta = 10$ [BED10], HR = 2.380; $p = 0.0084$). Worse in-field control was linked to lower prescription doses in squamous cell carcinomas (12 Gy × 4 or 10 Gy × 5 vs. 18 Gy or 20 Gy × 3: HR = 3.530; $p = 0.0447$), independent of GTV (HR = 1.014 per mL; $p = 0.0012$). No differences in in-field control were observed with the above dosing in adenocarcinomas ($p = 0.12$ and $p = 0.31$, respectively). To conclude, the combination of GTV, histology and radiation dose is an important predictor for local recurrence risk in the study population. The findings also suggest avoiding lower prescription doses (i.e., 12 Gy × 4 or 10 Gy × 5) for squamous cell carcinomas when it is safe. (p. 1549)

Programmed Death 1 Blockade With Nivolumab in Patients With Recurrent Malignant Pleural Mesothelioma



This single-center study evaluated nivolumab in 34 patients with recurrent malignant pleural mesothelioma (MPM). Partial response was observed in 8 patients at 12 weeks, and stable disease was found in another 8 patients, contributing to a disease control rate at 12 weeks of 47%. One partial response was observed at 18 weeks, and 4 patients had stable diseases for $>$ 6 months. The rate of treatment-related adverse events (AEs) of any grade was 76%, with fatigue and pruritus being the most common (29% and 15%, respectively). The rate of grades 3 and 4 treatment-related AEs was 26%, with pneumonitis, gastrointestinal disorders, and laboratory disorders being the most common. One treatment-related death was reported, as a result of pneumonitis, potentially triggered by concurrent amiodarone therapy. Tumor PD-L1 expression was found in 27% of samples but no association with treatment outcome was observed. In summary, the results suggest clinical efficacy and manageable safety profile of single-agent nivolumab in treating mesothelioma, in which PD-L1 expression does not predict response. (p. 1569)

Brigatinib in Patients With Alectinib-Refractory *ALK*-Positive NSCLC: A Retrospective Study



This multicenter, retrospective study investigated the second-generation anaplastic lymphoma kinase (ALK) inhibitor, brigatinib, in 22 patients with advanced, alectinib-refractory *ALK*-positive non-small cell lung cancer (NSCLC). Of 18 patients with measurable disease, 17% had confirmed objective responses, and 50% had stable disease. Patients achieved a median progression-free survival of 4.4 months with a median duration of treatment of 5.7 months. Five out of 9 patients, who had post-alectinib/pre-brigatinib biopsies, demonstrated an *ALK* I1171X or V1180L resistance mutation. Of these patients, 1 had a confirmed partial response and 3 had stable disease with brigatinib. One patient with a post-alectinib/pre-brigatinib biopsy showing an *ALK* G1202R mutation had progressive disease as the best overall response. Taken together, limited clinical activity was observed with brigatinib in alectinib-refractory *ALK*-positive NSCLC. More studies are warranted to determine biomarkers for brigatinib treatment and better treatment options for the study patient population. (p. 1530)

Research Watch

CNS Efficacy of Osimertinib in Patients With T790M-Positive Advanced Non—Small Cell Lung Cancer: Data From a Randomized Phase III Trial (AURA3)

The phase III AURA3 trial compared the CNS efficacy of osimertinib with platinum-pemetrexed in 419 patients with *EGFR* T790M—positive advanced NSCLC whose disease progressed on EGFR-tyrosine kinase inhibitor (EGFR-TKI) treatment. Measurable and/or non-measurable CNS lesions were found in 116 patients, including 46 with measurable CNS lesions. CNS objective response rate (ORR) was 70% with osimertinib and 31% with