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LARGE CELL NEUROENDOCRINE CARCINOMAS (LCNEC)
OF THE LUNG: PATHOLOGIC FEATURES, TREATMENT AND
OUTCOMES

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Aim: LCNEC is a rare thoracic malignancy, for which pathologic classification and
optimal therapies are debated. We report the largest series of stage IV LCNECs,
evaluating clinicopathologic features, treatment and survival.

Methods: Pts with stage IV LCNEC evaluated at MSKCC from 2006-2013 were
identified. Clinicopathologic and treatment data were collected. Radiologic RECIST
evaluation was performed for pts with existing diagnostic imaging. Pts with available
tissue underwent pathology re-review to confirm diagnosis, and potentially identify
features that could impact outcomes.

Results: 50 pts were identified (median age: 66 years; 62% male; 88% former/current
smokers). Common sites of metastasis: lymph nodes (n = 29); brain (n = 22); liver
(n = 13). 34% of pts had diagnostic molecular testing with PCR-based fragment
length analysis, mass spectrometry based assay for point mutation genotyping, and
ALK FISH testing: 24% had KRAS mutations (mtns) (n = 4/17; G12D, n = 2; G12C,
n = 1; Q61H, n = 1). No EGFR mtns or ALK rearrangements were noted. 33 pts had
archived tumor at MSKCC for central pathology re-review. The diagnosis of LCNEC
was confirmed in all but 2 cases, which were reclassified as SCLC and combined
SCLC/LCNEC (both brain metastases), respectively. Treatment data was available on
39 pts: 77% (n = 30) received first-line platinum(etoposide. 23% (n = 9) received
other regimens: plt/taxane (n = 4), plt/pemetrexed (n = 1), plt/pemetrexed/
bevacizumab(bev) (n = 1), temozolomide (n = 1)/bev (n = 1), clinical trial (n = 1).
Objective response rate was 32% with plt/etoposide by RECIST (95% CI: 16-52%).
Median OS was 12.2mos (range: 9-19.3mos) for all pts. Karnofsky performance status
<80 and LDH >250 were poor prognostic factors for OS on multivariate analysis
(p < 0.05).

Conclusions: Pts with stage IV LCNEC have low response to plt/etoposide treatment
and poor OS. KRAS mutations are commonly observed. Prospective studies are needed
to investigate optimum therapeutic strategies.

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