Baseline total metabolic tumor volume assessed by 18FDG-PET/CT predicts outcome in advanced melanoma patients treated with pembrolizumab

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Published in:
Annals of Oncology

Publication date:
2018

21P - Baseline total metabolic tumor volume assessed by 18FDG-PET/CT predicts outcome in advanced melanoma patients treated with pembrolizumab (ID 377)

Presentation Number
21P
Lecture Time
12:30 - 12:30
Speakers
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Session Name
Poster Display session
Location
Room B, Geneva Palexpo, Geneva, Switzerland
Date
14.12.2018
Time
12:30 - 13:00
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Abstract

Background

Pembrolizumab (PEMBRO) improves survival in patients (pts) with advanced melanoma (MEL). Baseline (BL) parameters that predict long-term benefit for PEMBRO treatment are under investigation.

Methods

Outcome data of pts with advanced MEL treated with PEMBRO at our institution were collected as part of a prospective therapeutically non-interventional trial. Objective responses were evaluated using the immune-related response criteria. Total metabolic tumor volume (TMTV) was assessed by 18-fluorodeoxyglucose positron emission tomography (18FDG-PET/CT) using MIM Encore Software®. TMTV was defined as the sum of all tumor-associated voxels with a standardized uptake value (SUV) higher than the mean SUV measured in a reference region in normal liver tissue + 3 standard deviations.

Results

BL 18FDG-PET/CT disease staging results were available for 69 pts. Median progression-free survival (mPFS) was 19 w (95% CI 9-29); median overall survival (mOS) was 130 w. A cut-off value of 90mL of BL TMTV defined a subpopulation with significantly worse PFS (mPFS 7 w [95% CI 4-9] vs 56 w [95% CI 0-118]; HR 19.10, $p<0.001$) and OS (mOS 21 w [95% CI 2-41] vs not reached; HR 46.14, $p<0.001$). Additionally, a history of brain metastases (HBM), C-reactive protein (CRP) >5 times upper limit of normal (>5xULN), lactate dehydrogenase (LDH) >1xULN, WHO Performance Status (WHO PS) ≥1 and number of metastatic sites ≥2 were associated with significantly shorter PFS and OS in univariate analysis (log rank $p<0.05$). In multivariate analysis (Cox multivariate logistic regression), a BL TMTV >90mL (HR 3.70 [95% CI 1.79-7.69]), HBM (HR 2.08 [95% CI 1.11-3.85]) and WHO PS≥1 (HR 2.08 [95% CI 1.12-3.85]) were significantly associated with shorter PFS; BL TMTV >90mL (HR 14.29 [95% CI 5.26-33.33]) and HBM (HR 2.56 [95% CI 1.23-5.26]) were significantly associated with shorter OS.

Conclusions

BL TMTV >90mL and HBM independently correlate with worse PFS and OS in pts with advanced MEL treated with PEMBRO. Elevated BL CRP and LDH values overlap with, but are inferior to TMTV as predictive biomarkers for outcome of PEMBRO treatment. Confirmation of these results is under investigation in an independent second cohort.

Legal entity responsible for the study

Universitair Ziekenhuis Brussel, Brussels, Belgium.

Funding

Has not received any funding.

Disclosure

All authors have declared no conflicts of interest.