

1641 TiP - Adjuvant nivolumab with chemotherapy in pleural mesothelioma – the NICITA trial

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Background

- There is no approved treatment for early-stage malignant pleural mesothelioma (MPM) yet.
- Multimodal treatment approaches preferably by extended pleurectomy/decortication (eP/D), if feasible, in combination with hyperthermic intrathoracic chemoperfusion (HITOC), and neoadjuvant or adjuvant chemotherapy has become standard practice at major academic centers in Germany.¹
- Efficacy has been reported for PD-1 or PD-L1 inhibitor in combination with chemotherapy.²⁻⁴
- Chemotherapeutic agents can induce immunogenic effects in the tumor microenvironment. Thus, synergistic effects are expected when combining chemotherapy with immune checkpoint inhibitors.⁵

Objectives

Primary objective: To determine whether addition of nivolumab to platinum-based adjuvant chemotherapy with pemetrexed and subsequent administration of nivolumab as maintenance therapy improves the time-to-next-treatment (TNT)

Primary Endpoint: TNT, safety (acc. to NCI-CTCAE v 5.0) and tolerability

Secondary Endpoint: OS, PFS, proportion of patients with treatment beyond progression (TBP), duration of TBP in this population, quality of life (QoL) (LCSS-Meso, EQ-5D)

Exploratory Endpoint: Biomarker exploration

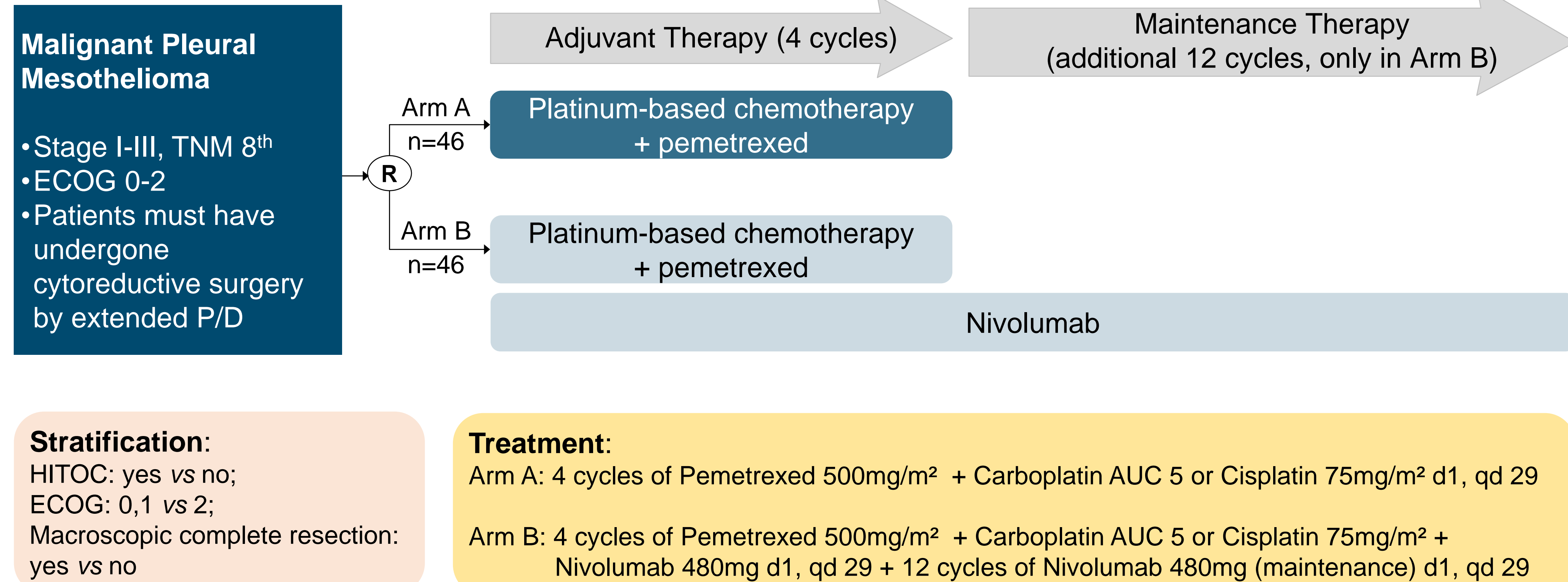
Key inclusion criteria

- Histologically proven initial diagnosis of MPM of epithelioid subtype
- Stage I-III (TNM 8th Edition). Patients are only included with a completeness of cytoreduction score (CC score) <3 (i.e., residual tumor nodules ≤2.5 cm).⁶
- Patients must have undergone cytoreductive surgery with curative intent consisting of eP/D ± HITOC.
- ECOG performance status 0-2

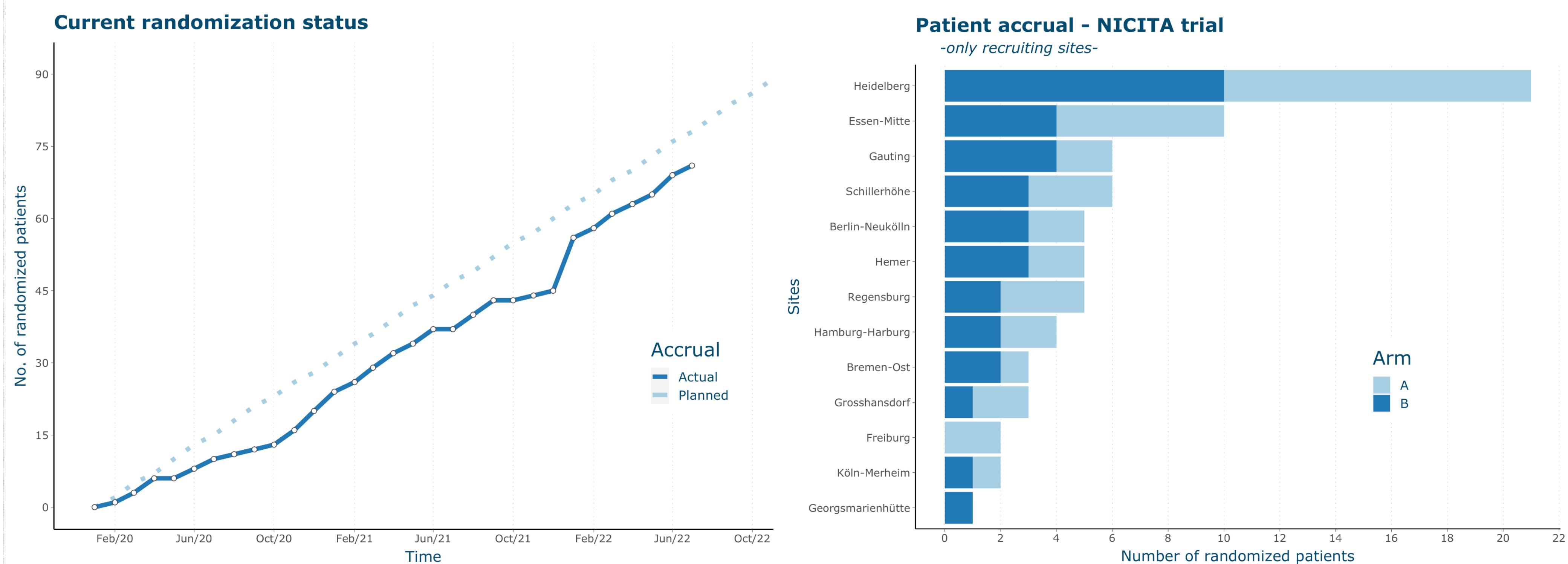
Key exclusion criteria

- Metastatic disease
- Previous drug therapy against MPM, prior immune-oncological treatment
- Post-operative hospitalization > 6 weeks
- Subjects with interstitial lung disease that is symptomatic or may interfere with the detection or management of suspected drug-related pulmonary toxicity.

Study design: Multicenter, Open-label, randomized phase II study



Accrual: As of 1st Aug 2022, thirteen sites are recruiting. 71 of 92 planned patients have been enrolled.



This trial is conducted by the Young Medical Oncologists (AIO-YMO) Group in cooperation with the Thoracic Oncology team of Working Group for Internal Oncology (AIO), German Cancer Society, sponsored by the Institute of Clinical Cancer Research (IKF), and funded by an unrestricted grant from Bristol Myers Squibb GmbH & Co.KGaa (BMS).

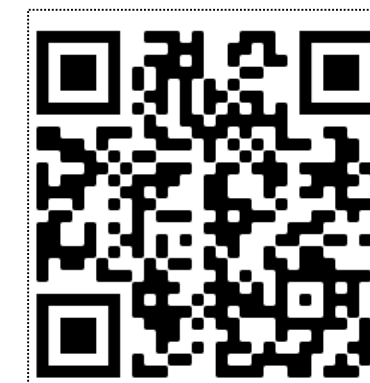
Statistical analysis

Sample size justification: the recruitment of n=46 patients to each arm appears feasible in a multicenter setting within a recruitment period of 24 months. A low drop-out rate of 13% is expected resulting in n=40 patients to be analyzed per arm. With this sample size, it is possible to descriptively compare and adequately describe the tested treatment options as deduced from the precision of the median TNT confidence interval estimate.

For the description of the primary endpoint TNT, the Kaplan-Meier method will be used. The primary efficacy analysis will be based on the intention-to-treat principle. The median TNT will be described using 95% confidence intervals. Furthermore, to compare the TNT between the two treatment groups, a descriptive log-rank test will be performed. Secondary efficacy endpoints will be described and compared between group with effect sizes and corresponding 95% confidence intervals.

Trial registry numbers

ClinicalTrials.gov ID: NCT04177953;
 EudraCT: 2019-002466-13;
 AIO Study Number: AIO-TRK/YMO-0419



Conflict of interest

Rajiv Shah reports speaker's honoraria from Roche, AstraZeneca and institutional research funding from BMS.

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