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3-year survival with neoadjuvant-adjuvant pembrolizumab from SWOG S1801

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Background

Data from two large randomized trials have shown neoadjuvant (Neo) immunotherapy for resectable melanoma (mel) improves event-free survival (EFS) over adjuvant (Adj) therapy. Adj therapy improves recurrence-free survival (RFS) over placebo in resectable mel but has no effect on overall survival (OS).

Methods

SWOG S1801 was a randomized phase 2 study in 345 pts of Adj pembrolizumab (pem) versus Neo-Adj pem for resectable, clinically detectable mel. Data were analyzed as of May 9, 2025 for updated endpoints.

Results

At a median follow-up of 44 months EFS benefit was maintained in the Neo group (HR 0.67, 95% CI 0.47 – 0.94). 3-year EFS was 68% in the Neo group (95% CI 62-72%) and 55% in the Adj group (95% CI 48-64%). With 32 death events in the Neo group and 47 deaths in the Adj group, 3-year OS was 84% versus 73% (HR 0.65, 95% CI 0.42 – 1.02). In an exploratory subgroup of 33 pts with resectable stage IV mel, EFS and OS demonstrate a trend toward improvement in the Neo-Adj group with only 1 event for EFS and 0 events for OS compared to 10 events for EFS and 5 deaths in the Adj group (HR for EFS 0.08 95% CI 0.01-0.61, HR for OS could not be estimated with 0 events in Neo-Adj group). EFS and OS were similar between treatment groups in pts harboring *BRAF* mutation. In the subgroup of Neo-Adj pts that did not undergo surgery (n=18) one pt did not undergo surgery due to toxicity and was still alive without recurrence at 35 months. 2 pts did not undergo surgery due to radiographical CR; 1 progressed at 5.2 months and died at 3.6 yr and 1 was alive without recurrence at 5 yr. 2 Two pts did not have surgery due to co-morbidities and/or COVID-related constraints at the hospital – both died in less than a year after going off protocol. The remaining 13 pts did not have surgery due to progression of mel rendering them unresectable - 6 have died, 3-year OS = 61%. With longer follow-up, grade 3/4 toxicity was noted in n=35 (20%) in Neo-Adj group and 29 (17%) in the Adj group (p=0.41). One grade 5 myocarditis was observed in the Adj group.

Conclusions

At a median follow-up of 3.7 years Neo-Adj pem maintains EFS benefit over Adj pem in resectable mel. Median OS remains immature but continues to show a trend toward benefit with Neo-Adj pem.

Clinical trial identification

NCT03698019.

Legal entity responsible for the study

SWOG.

Funding

SWOG; MSD provided drug supply and funding for translational medicine endpoints.

Disclosure

S.P. Patel: Financial Interests, Personal, Advisory Board: TriSalus, Novartis, BMS, Cardinal Health, IO Biotech, Pfizer, OncoSec, Scancell; Financial Interests, Institutional, Invited Speaker: Pfizer, Clinical Education Alliance, Vindico Medical; Financial Interests, Personal, Invited Speaker, Non-promotional speaker: BMS, MSD; Financial Interests, Personal, Other, IDMC member: Ideaya; Financial Interests, Personal, Other, Ad Hoc Consulting: Novartis; Financial Interests, Institutional, Advisory Board: Replimune, Veda Trials, MSD, Natera; Financial Interests, Institutional, Trial Chair: Provectus Biopharmaceuticals; Financial Interests, Institutional, Local PI: Lyvgen, InxMed, Foghorn Therapeutics, Ideaya, Novartis, Seagen, Syntrix Bio; Financial Interests, Institutional, Steering Committee Member: TriSalus Life Sciences; Non-Financial Interests, Member: ASCO, AACR, International Society of Ocular Oncology, Society for Melanoma Research; Non-Financial Interests, Leadership Role: SWOG; Non-Financial Interests, Member, Neoadjuvant Task Force Co-Chair: SITC. E. Buchbinder: Financial Interests, Personal, Advisory Board: BMS, Iovance, Merck, Zola, Obsidian, Anaveon, Werewolf, Immunocore; Financial Interests, Institutional, Coordinating PI: Genentech, Partners therapeutics; Other, Spouse employment: Takeda. C. Devoe: Non-Financial Interests, Other, Site PI on clinical trial CBP-1019-101: Coherent Biopharma; Non-Financial Interests, Other, Site PI on clinical trial DEK-DKK1-P207 (DEFIANCE trial): Leap Therapeutics; Non-Financial Interests, Other, Site PI for MK-7684A-010: Merck; Non-Financial Interests, Other, Site PI for ELI-002-001 (AMPLIFY-201) & ELI-002-201 (AMPLIFY-7P): Elicio Therapeutics. V.K. Sondak: Financial Interests, Personal, Advisory Board: Merck, Bristol Myers Squibb; Financial Interests, Personal, Other, Independent Data Safety Monitoring Committee: Mural Oncology; Financial Interests, Institutional, Research Grant, Research grant to institution: Turnstone Biologics; Financial Interests, Institutional, Coordinating PI, Per patient funding to institution to support clinical trial: Skyline DX; Financial Interests, Institutional, Local PI, Research grant to institution: Neogene Therapeutics. A. Ribas: Financial Interests, Personal, Advisory Board, Honoraria for consulting: Amgen, Merck; Financial Interests, Personal, Advisory Board, Member of the Scientific Advisory Board: Apricity, Appia, Arcus, Compugen, Immpact, Lutris, MapKure, Merus, Synthekine, Tango; Financial Interests, Personal, Member of Board of Directors, Member of the Board of Directors: Arcus, Lutris; Financial Interests, Personal, Stocks/Shares, Stock ownership: 4C Biomed, Apricity, Appia, Arcus, Compugen; Financial Interests, Personal, Stocks/Shares: Highlight, Lutris, Compugen, Merus, Synthekine, Tango, Kite-Gilead, Arcus, Advaxis, CytomX, 4C Biomed; Financial Interests, Personal, Advisory Board: Arsenal Bio; Non-Financial Interests, Advisory Role, Member of the scientific advisory board: Highlight, Immunesensor, Inspirna, Pluto. All other authors have declared no conflicts of interest.