1

Gynecologic Cancer InterGroup (GCIG) Consensus: In 2011, the GCIG published a consensus statement recommending **PFS as the preferred primary endpoint** for phase III trials in first-line therapy of ovarian cancer.

Stuart, G. C., et al. (2011). 2010 Gynecologic Cancer InterGroup (GCIG)

FDA Guidance: The U.S. Food and Drug Administration (FDA) has recognized **PFS as an acceptable endpoint** for ovarian cancer trials, particularly in the context of maintenance therapy.

FDA Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (2018)

PFS endpoints allow for shorter trial durations and smaller sample sizes compared to OS endpoints, facilitating more efficient drug development.

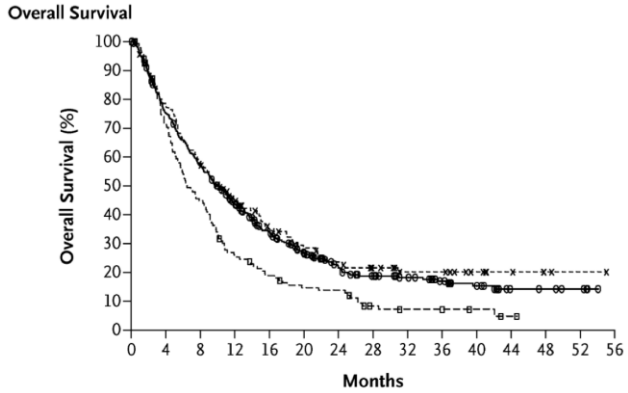
Matulonis, U. A., et al. (2016). Ovarian cancer: state of the science. Nature Reviews Cancer, 16(5), 265-282.

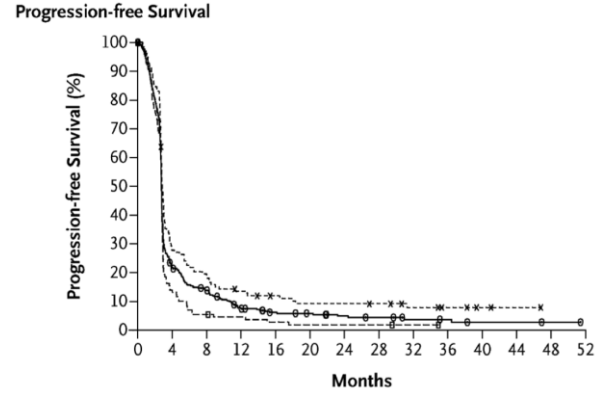
PFS is widely accepted as preferred primary endpoint.

Published in final edited form as:
N Engl J Med. 2010 August 19; 363(8): 711–723. doi:10.1056/NEJMoa1003466.

Improved Survival with Ipilimumab in Patients with Metastatic Melanoma

Minimal PFS benefit but significant OS improvement





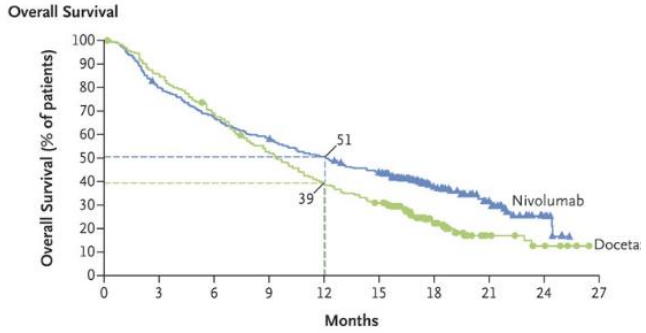
ORIGINAL ARTICLE

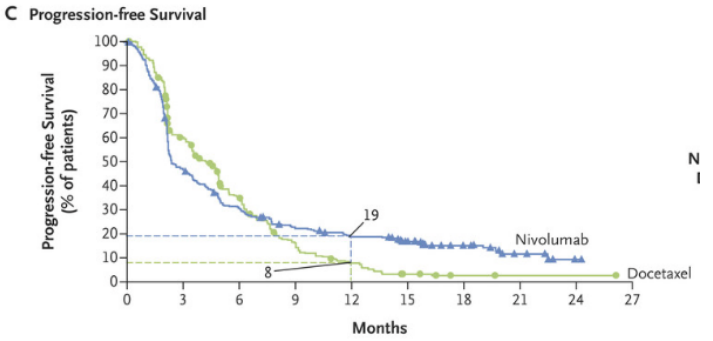
Nivolumab versus Docetaxel in Advanced Nonsquamous Non–Small-Cell Lung Cancer

Authors: Hossein Borghaei, D.O., Luis Paz-Ares, M.D., Leora Horn, M.D., David R. Spigel, M.D., Martin Steins, M.D., Ph.D., Neal E. Ready, M.D., Ph.D., Laura Q. Chow, M.D., +20, and Julie R. Brahmer, M.D. Author Info & Affiliations

Published October 22, 2015 | N Engl J Med 2015;373:1627-1639 | DOI: 10.1056/NEJMoa1507643

A greater OS benefit than PFS benefit





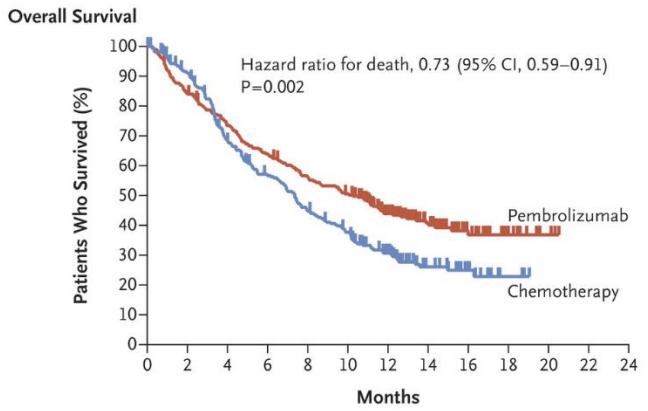
ORIGINAL ARTICLE

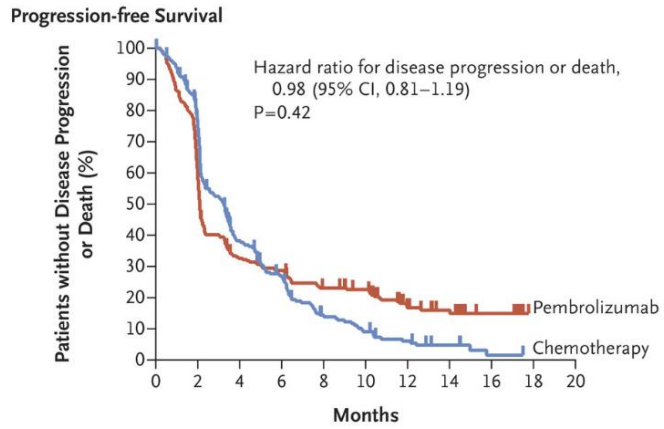
Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma

Authors: Joaquim Bellmunt, M.D., Ph.D., Ronald de Wit, M.D., Ph.D., David J. Vaughn, M.D., Yves Fradet, M.D., Jae-Lyun Lee, M.D., Ph.D., Lawrence Fong, M.D., Nicholas J. Vogelzang, M.D., +13, for the KEYNOTE-045 Investigators* Author Info & Affiliations

Published March 16, 2017 | N Engl J Med 2017;376:1015-1026 | DOI: 10.1056/NEJMoa1613683 | VOL. 376 NO. 11

an OS benefit without a significant PFS improvement.





nature communications

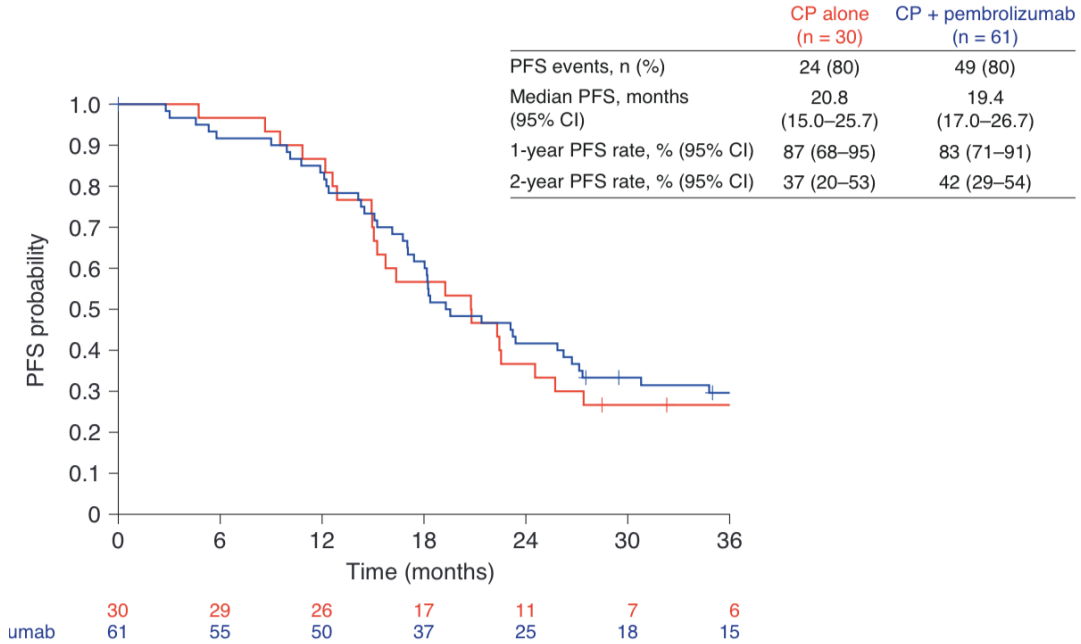
Article

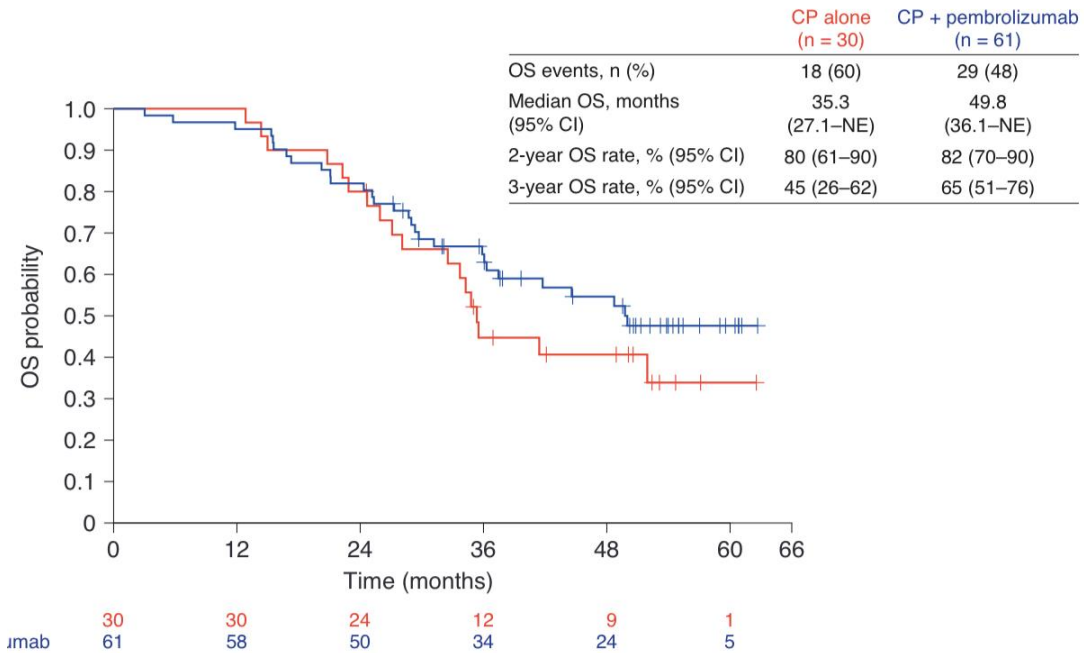
https://doi.org/10.1038/s41467-024-46999-x

Neoadjuvant and adjuvant pembrolizumab in advanced high-grade serous carcinoma: the randomized phase II NeoPembrOV clinical trial

The median progression-free survival (PFS) was similar between the two treatment arms, with 20.8 months for standard care and 19.4 months for the investigational arm.

However, overall survival (OS) favored the investigational arm, with a median OS of 49.8 months compared to 35.3 months in the standard care arm.





Konstantinopoulos, P. A., et al. (2020). Single-arm phases 1 and 2 trial of niraparib in combination with pembrolizumab in patients with recurrent platinum-resistant ovarian carcinoma. JAMA Oncology, 6(8), 1239-1247.

HGSOC, particularly those with BRCA mutations or homologous recombination deficiency (HRD), may be more likely to benefit from immunotherapy. This is partly due to their higher mutational burden and potential for increased neoantigen production.

Takaya, H., et al. (2020). Therapeutic strategies for ovarian clear cell carcinoma from a pathogenetic perspective. Cancers, 12(7), 1797.

Clear cell ovarian carcinoma: This subtype has shown some promise in responding to immunotherapy, possibly due to its association with microsatellite instability (MSI) in some cases.

Ghisoni, E., et al. (2019). Ovarian cancer immunotherapy: turning up the heat. International Journal of Molecular Sciences, 20(12), 2927.

Endometrioid ovarian carcinoma: Some endometrioid ovarian cancers, especially those with mismatch repair deficiency (dMMR) or high microsatellite instability (MSI-H), may be more responsive to immunotherapy.

Q1 OS benefit vs PFS benefit

Progression-free survival (PFS) exhibits suboptimal performance as the surrogate endpoint for overall survival (OS) in trials studying immune checkpoint inhibitors (ICIs).

Is this phenomenon inherent to the characteristics of immunotherapy, or is it expected to vary depending on the mechanism of action, even among different immune checkpoint inhibitors?

Q2 Immunotherapy has not yet shown very significant effects in ovarian cancer treatment. Is there evidence to expect different effects based on cell subtypes? If so, which cell subtype is most likely to benefit from immunotherapy?"

Example,
Serous with BRCA m, HRD
Endometrioid , clear cell with MMRd, MSI H