

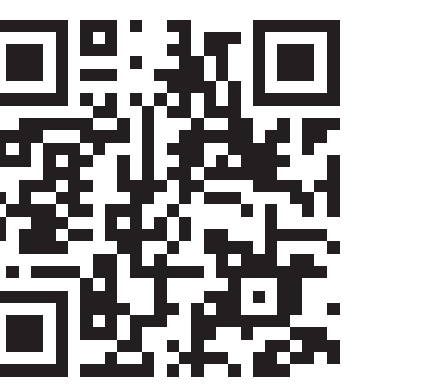
CheckMate 77T: A Double-Blind Phase 3 Trial of Neoadjuvant Nivolumab Plus Chemotherapy Followed by Adjuvant Nivolumab in Resectable Non-Small Cell Lung Cancer

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Background

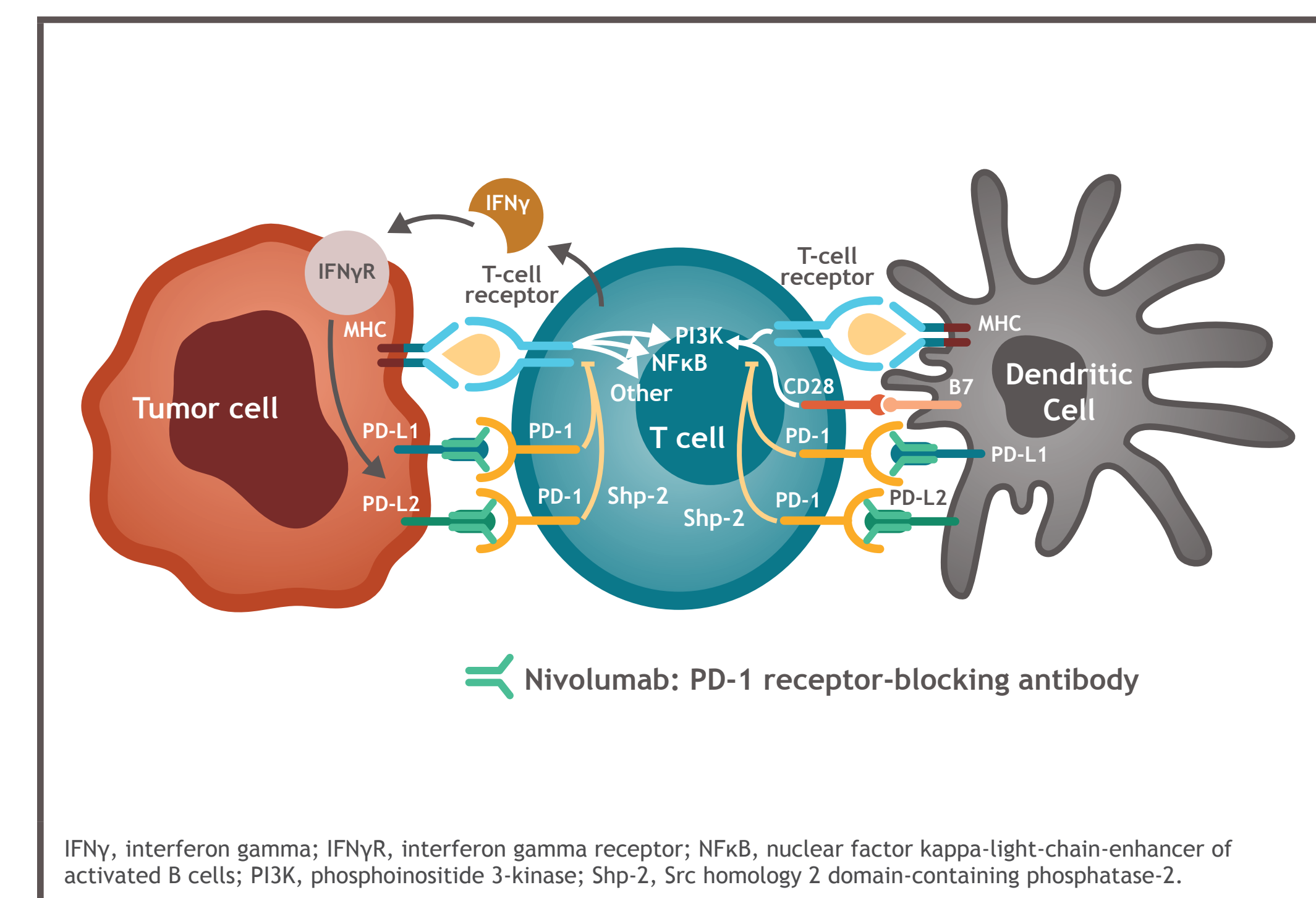
Unmet medical needs in early or localized resectable non-small cell lung cancer (NSCLC)

- Lung cancer is the leading cause of cancer death worldwide¹
 - NSCLC comprises the majority of lung cancer cases (~ 85% in the United States)²
 - Up to 20%-25% of patients with NSCLC present with early or localized disease amenable to surgery³
- Although potentially curative for stage IIA-IIIb disease, surgery historically results in 5-year overall survival (OS) rates < 50%⁴
 - A rational approach to improve OS in these patients is to eradicate micrometastatic disease and minimize relapse risk with adjuvant or neoadjuvant therapy^{5,6}
 - However, conventional neoadjuvant or adjuvant chemotherapy provides only a 5% absolute improvement in OS at 5 years^{7,8}
 - New therapeutic approaches for patients with early or localized NSCLC are needed

Immune checkpoint inhibition with nivolumab

- Programmed death (PD)-1, an immune checkpoint molecule that is highly expressed on activated T cells, regulates T-cell function during inflammation by binding to its ligands, PD ligand 1 (PD-L1) and PD ligand 2 (PD-L2), on tissue cells and antigen-presenting cells⁹
 - Engagement of PD-1 on tumor-infiltrating T cells by PD-L1 or PD-L2 on tumor cells leads to T-cell inhibition and tumor immune evasion⁹
- Nivolumab is a fully human PD-1 immune checkpoint inhibitor antibody that blocks the binding of PD-1 to PD-L1 / PD-L2, thereby abrogating negative signaling and restoring antitumor T-cell activity (Figure 1)¹⁰⁻¹²
 - Nivolumab, in combination with ipilimumab, is indicated in the United States for the first-line treatment of adult patients with metastatic NSCLC whose tumors express PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations¹³
 - Nivolumab as monotherapy is approved in the United States,¹³ the European Union,¹⁴ and other countries for the treatment of patients with metastatic NSCLC whose disease has progressed on or after chemotherapy, as well as for the treatment of patients with other tumors in various countries

Figure 1. Nivolumab mechanism of action

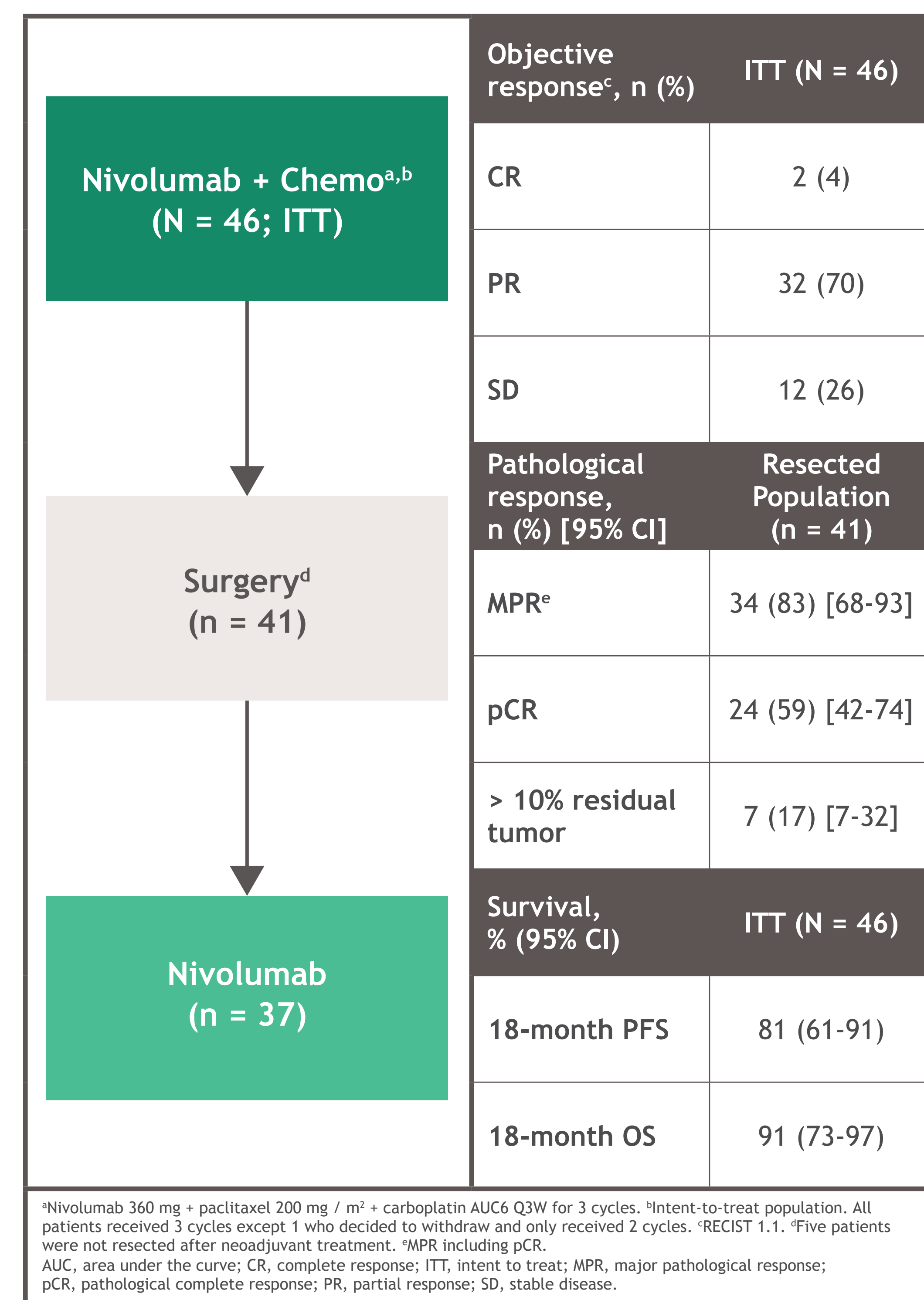


Study Rationale

Nivolumab combined with chemotherapy as perioperative therapy

- Combining cytotoxic chemotherapy with a PD-1 inhibitor therapy may augment the antitumor immune response through cell-death induced increased tumor antigenicity and reduction of Treg-mediated immune suppression^{15,16}
- Early phase trials using major pathologic response (MPR; \leq 10% viable tumor in resected tumor specimens) indicate that nivolumab-based regimens have the potential to deepen pathological responses and extend survival in this setting¹⁷⁻¹⁹
- Neoadjuvant nivolumab plus chemotherapy followed by adjuvant nivolumab exhibited encouraging response and preliminary survival outcomes in patients with resectable stage IIIa NSCLC in the single-arm phase 2 NADIM trial (Figure 2)¹⁹
 - No patients withdrew preoperatively due to toxicity¹⁹
 - 18-month progression-free survival (PFS): 81% (95% CI: 61%-91%)¹⁹
 - 18-month OS: 91% (95% CI: 73%-97%)¹⁹

Figure 2. Efficacy of neoadjuvant nivolumab plus chemotherapy followed by adjuvant nivolumab in stage IIIa resectable NSCLC (NADIM study)¹⁹



Study Design

- CheckMate 77T (NCT04025879) is a phase 3, randomized, double-blind trial evaluating neoadjuvant nivolumab plus chemotherapy followed by adjuvant nivolumab vs neoadjuvant placebo plus chemotherapy followed by adjuvant placebo in resectable early stage NSCLC (Figure 3)
- Key inclusion and exclusion criteria are listed in Table 1

Figure 3. CheckMate 77T study design

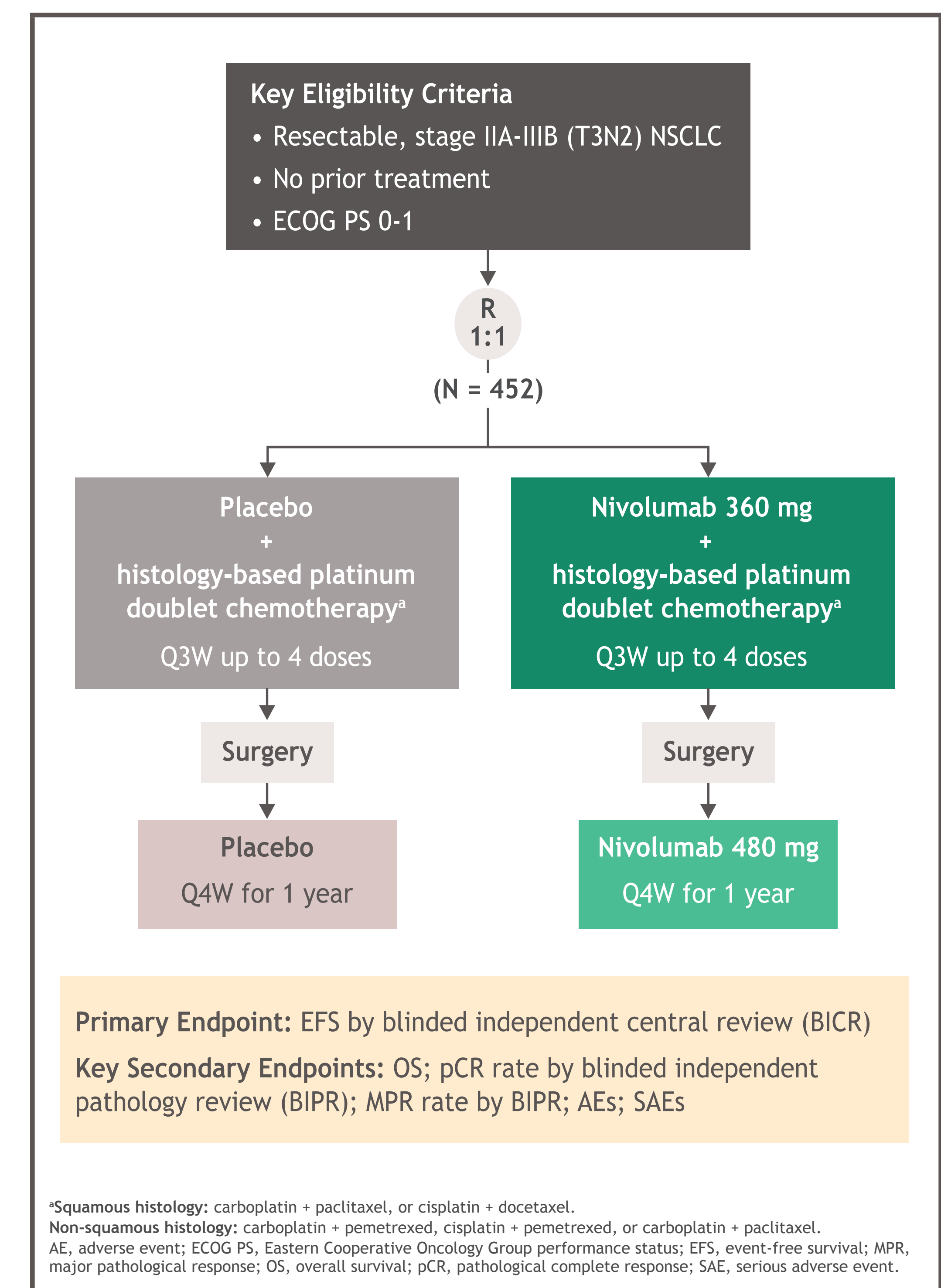


Table 1. Select CheckMate 77T inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Histologically confirmed, stage IIA-IIIb, resectable NSCLC	EGFR or ALK mutations
ECOG PS 0-1	Brain metastasis
Eligibility for complete lung cancer resection	Prior systemic anti-cancer treatment or radiotherapy in NSCLC
	Active, known, or suspected autoimmune disease

ECOG PS, Eastern Cooperative Oncology Group performance status.

Key Endpoints

Primary endpoint

- EFS by BICR

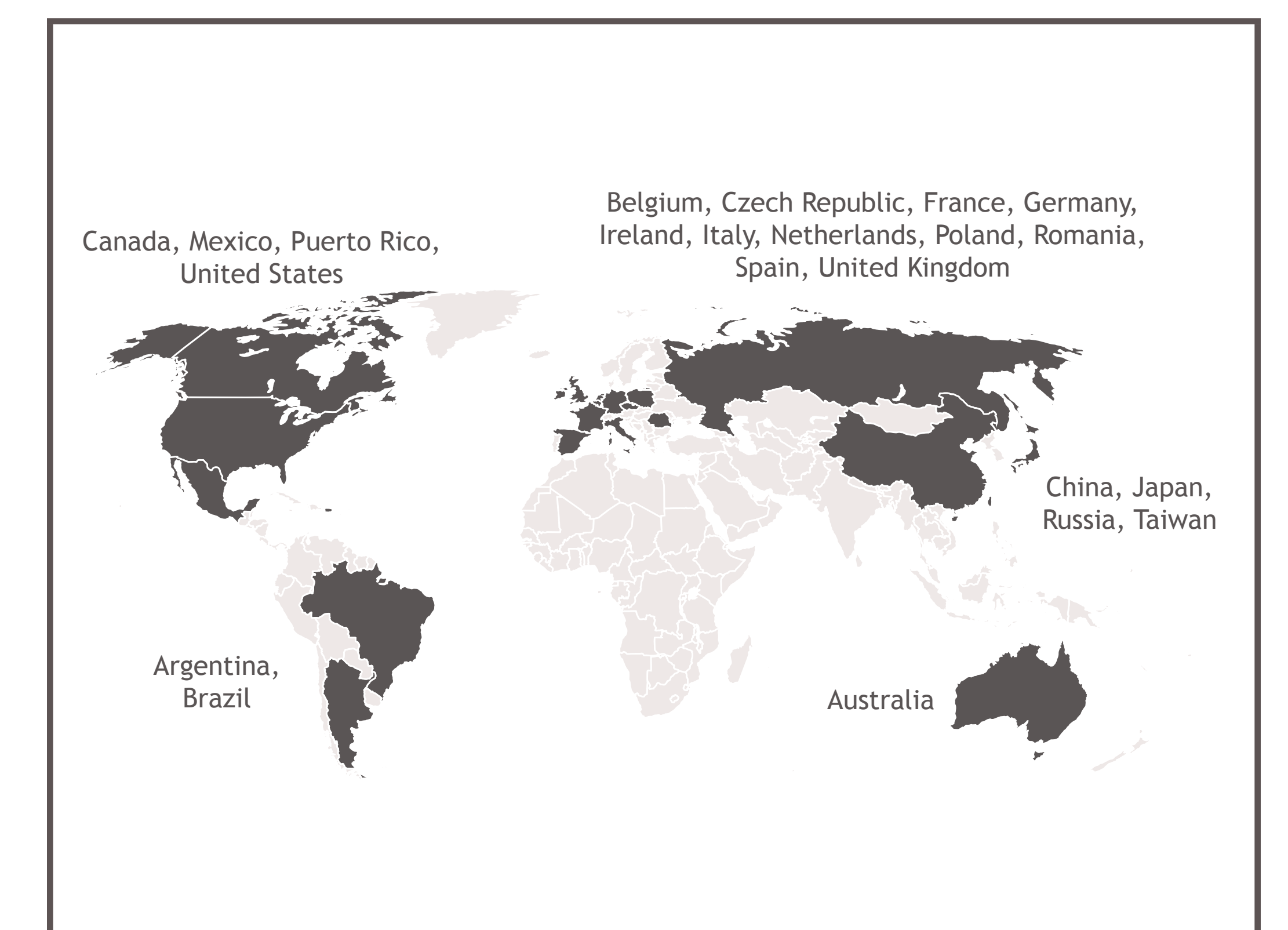
Secondary endpoints

- OS
- pCR rate by BIPR
- MPR rate by BIPR
- Safety and tolerability

Study Sites and Dates

- 115 study sites in 21 countries (Figure 4)
- Study start date: September 2019
- Estimated primary completion date: May 2023
- Estimated study completion date: September 2024

Figure 4. CheckMate 77T study sites



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