

EP 11.26: Phase-2 randomized-clinical-trial of low-dose nivolumab and low-dose chemotherapy in patients of advanced NSCLC with poor PS (ImPACT-I)

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INTRODUCTION

- ECOG performance status ≥ 2 is observed in up to 30% of patients with advanced NSCLC.
- Poor PS may be associated with high disease burden, comorbidities, advanced age, and impaired nutritional status, resulting in limited treatment options.
- Immune checkpoint inhibitors (ICIs) have shown only modest efficacy in patients with poor PS.
- The high cost of ICIs further limits their accessibility in India and other low- and middle-income countries (LMICs).
- There is an unmet need for effective, tolerable, and affordable treatment strategies for this difficult-to-treat population.
- This Phase II randomized study evaluates the feasibility of combining low-dose nivolumab with low-dose chemotherapy in carefully selected patients with advanced NSCLC and poor PS.
- The study aims to explore an adaptive and economically viable treatment approach that may improve outcomes while maintaining treatment feasibility and tolerability.

Study Objectives:

1. Evaluation of efficacy of low dose nivolumab in combination with low dose chemotherapy in terms of 6 months PFS rates in patients of advanced NSCLC with poor PS in comparison to low dose chemotherapy alone
2. Evaluation of objective response rates, toxicities, overall survival and change in quality of life with the proposed treatment regimen.
3. Correlation of PDL1 expression to predict the benefit of addition of low dose nivolumab to chemotherapy

METHODS

Study Design;

Multicentric, open-label, phase 2 randomized clinical trial using Simon phase 2 design.



Eligibility:

Age: 18 years and above, Histologically or cytologically confirmed advanced NSCLC, ECOG performance status of 2 or more, Charlson comorbidity score of ≤ 9 , adequate organ function and serum albumin ≥ 3.5 gm/dl or more



Randomization (1:1):

35 patients/arm, Total N = 70



Treatment Arms:

Arm A – Experimental

Low-dose nivolumab 20 mg IV q21 days, Low-dose paclitaxel 60 mg/m² weekly $\times$ 6 weeks
If PS improves: carboplatin AUC 2 added.
Maintenance nivolumab $\pm$ pemetrexed

Arm B – Control

Same low-dose chemotherapy regimen without nivolumab
Maintenance chemotherapy as applicable



Primary Endpoints

6-month progression-free survival (PFS) rate



Secondary Endpoints:

Overall response rate (ORR), overall survival (OS), quality of life (QoL), toxicities as per CTCAE v 5.21



Statistical design and Assumptions:

Simon Phase II design for randomized trials
Target 6-month PFS: 40%



Status:

Enrollment started May 2025

TRIAL IN PROGRESS

Study Schema

- Age > 18 years
- Histologically or cytologically confirmed advanced NSCLC
- ECOG performance status of 2 or more
- Charlson comorbidity score of ≤ 9
- Measurable disease per RECIST v1.1
- Adequate organ function
- Serum albumin > 3.5 gm/dl

1:1
Randomization

Arm A
Nivolumab 20 mg q 3 weekly
+
Paclitaxel 60 mg/m² weekly
For 6 weeks

PS improves to 2 or less

Nivolumab 20 mg q 3 weekly
Paclitaxel 60 mg/m² D1,8,15
Q 3 weekly
For 4 cycles

Maintenance
Nivolumab 20 mg q 3 weekly
+/-
Pemetrexed 500 mg/m² q 3 weekly
(only for non squamous)
Till disease progression or
intolerance

PS doesn't improve

Nivolumab 20 mg q 3 weekly
Paclitaxel 60 mg/m² D1,8,15
Q 3 weekly
Continued till 4 cycles /
deterioration in PS/ intolerance

Maintenance (optional)
Nivolumab 20 mg q 3 weekly
+/-
Pemetrexed 500 mg/m² q 3 weekly
(only for non squamous)
Till disease progression or
intolerance

PS improves to 2 or less

Paclitaxel 60 mg/m² D1,8,15
Carboplatin AUC 2 D1,8,15
Q 3 weekly
For 4 cycles

Pemetrexed 500 mg/m² q 3 weekly
(only for non squamous)
Till disease progression or
intolerance

PS doesn't improve

Paclitaxel 60 mg/m² D1,8,15
Q 3 weekly
Continued till 4 cycles /
deterioration in PS/ intolerance

Pemetrexed 500 mg/m² q 3 weekly
(only for non squamous)
Till disease progression or
intolerance

REFERENCES AND ACKNOWLEDGEMENTS

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