

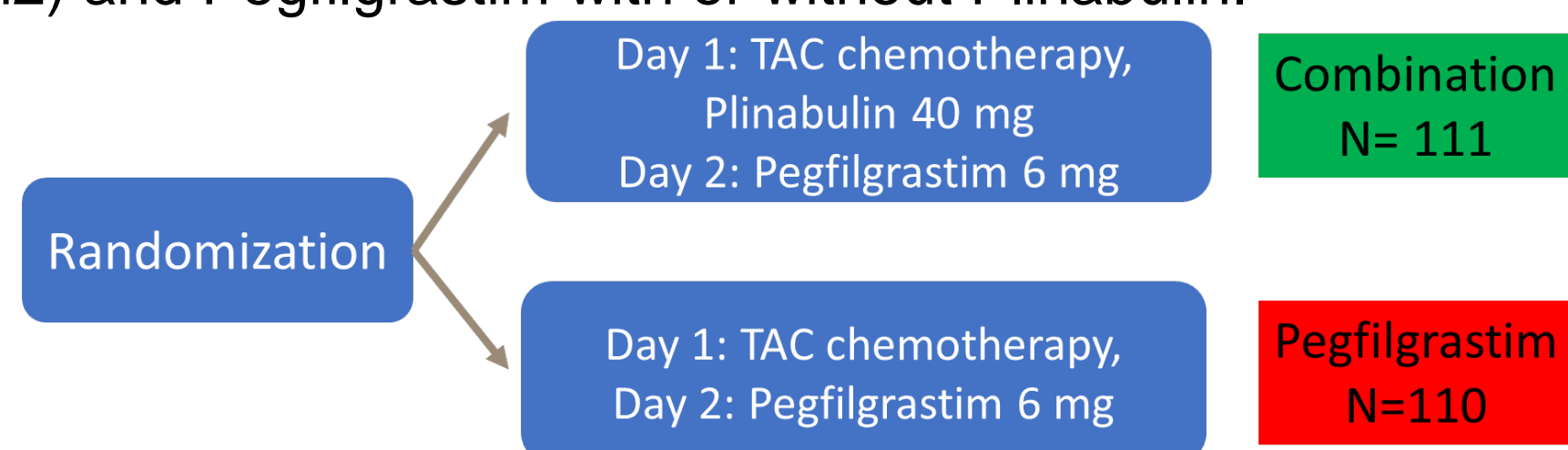
ESMO #3627 : Prediction of Febrile Neutropenia , Hospitalization Rates, and Infection Rates in Chemotherapy-Induced Neutropenia Patients Treated with the Plinabulin and Pegfilgrastim Combination (Plin+Peg) using a Meta-Analysis - based Tool

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INTRODUCTION

- Plinabulin is a novel non-G-CSF small molecule for the prevention of Chemotherapy (Chemo)-Induced Neutropenia (CIN)
 - Plinabulin has a fast onset Mechanism of Action (MoA) in the first week of the Chemo cycle, which is complementary to the slow onset MoA of G-CSF in the second week of the Chemo Cycle.
 - This was the rationale to combine Plinabulin with Pegfilgrastim for CIN
- In the Phase 3 trial PROTECTIVE-2 (NCT03294577), the Plinabulin +Pegfilgrastim combination had superior CIN- preventive efficacy versus Pegfilgrastim alone.
 - Grade 4 neutropenia frequency (Gr4N) was 86% for Pegfilgrastim alone and 68% for the Plinabulin/ Pegfilgrastim combination ($p < 0.0015$)
 - Days of severe neutropenia (DSN) ($p = 0.03$) and absolute neutrophil count nadir ($p = 0.0002$) were significantly superior with the Plinabulin/ Pegfilgrastim combination (Blayney ASCO 2021).
- PROTECTIVE-2 was a global, multicenter, randomized, double-blind study to evaluate severe neutropenia in Early-Stage Breast Cancer patients, receiving TAC (Docetaxel 75 mg/m², Doxorubicin 50 mg/m², Cyclophosphamide 500 mg/m²) and Pegfilgrastim with or without Plinabulin.

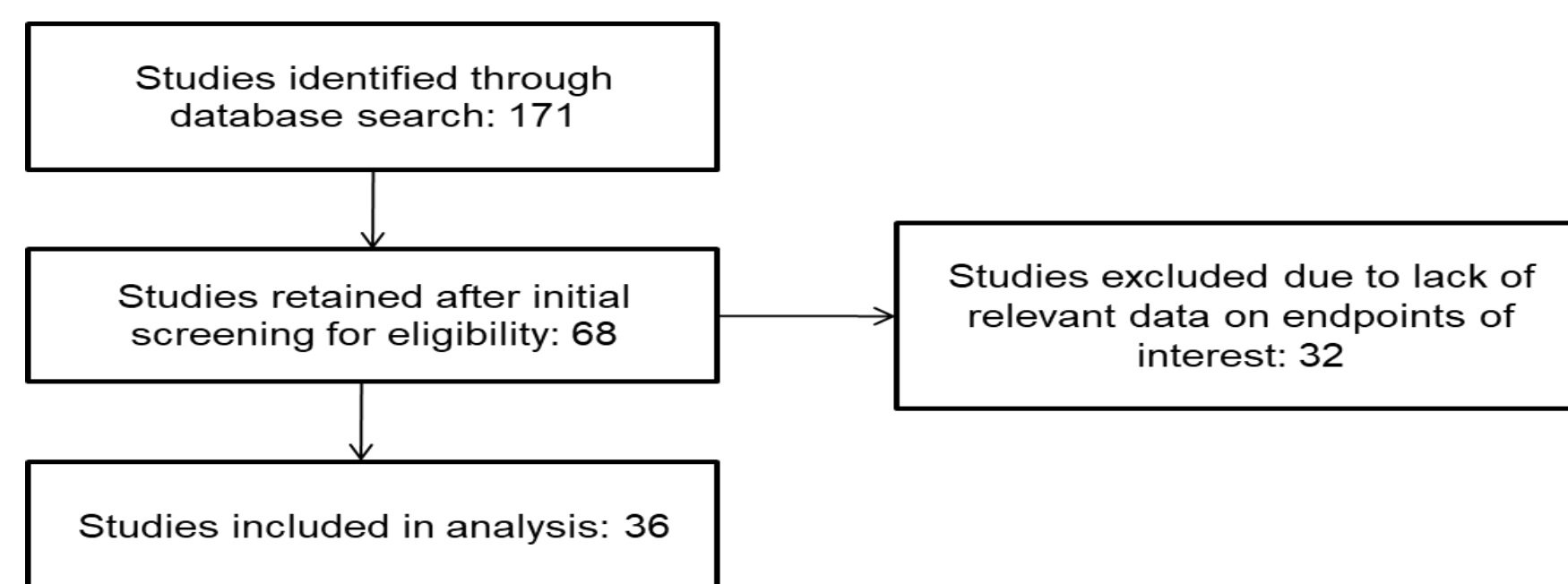


OBJECTIVE

- The PROTECTIVE-2 Study was conducted in an Early-Stage Breast Cancer setting using TAC chemotherapy. The observed effect size for Gr4N frequency by adding Plinabulin to Pegfilgrastim was a reduction from 86% with Pegfilgrastim alone, to 68% with the Plinabulin/Pegfilgrastim combination. We asked the question of what impact a Gr4N reduction from 86% to 68% would have on CIN outcomes (FN, DSN, Hospitalization Rate, Infection Rate) in a setting of “All Chemotherapies and in All Cancers” .
- This may provide insights in how the Plinabulin/Pegfilgrastim combination may perform in a “Real World” setting.

METHODS

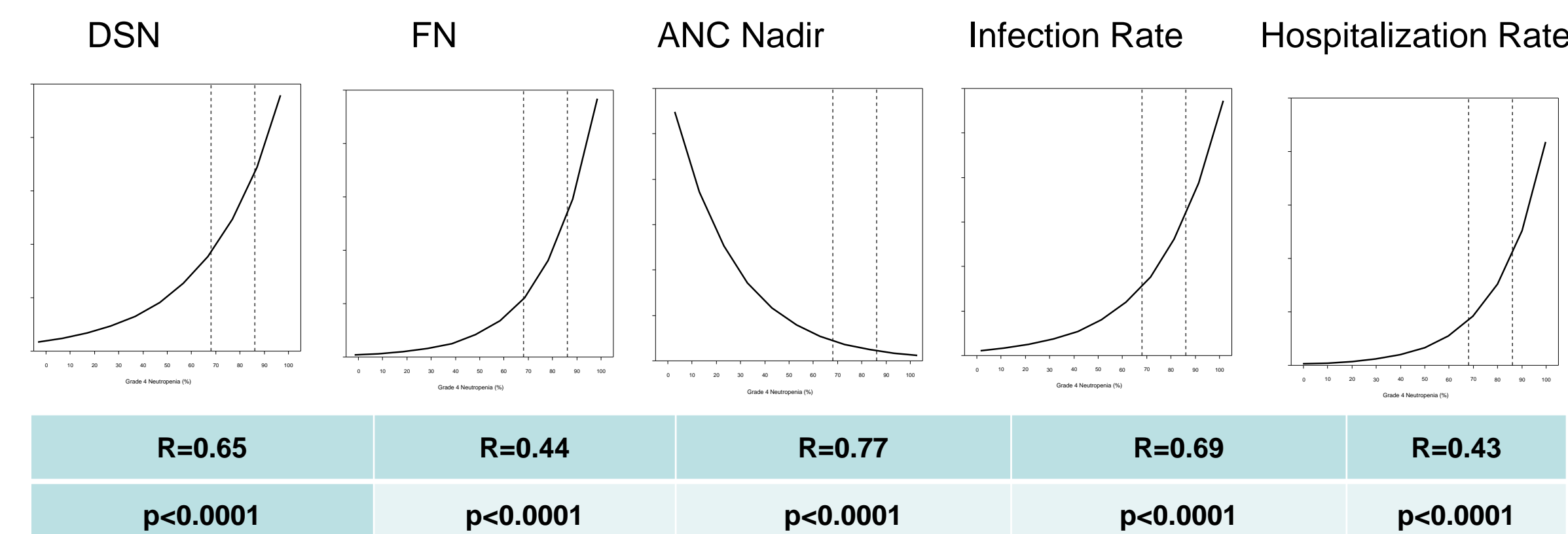
- A meta-analysis combining data from published CIN clinical trials and the clinical trial datasets from the novel CIN -preventive agent plinabulin was performed.
- Literature search terms included:
 - Grade 4 neutropenia,
 - Severe neutropenia,
 - Chemotherapy-induced neutropenia (CIN),
 - Febrile neutropenia (FN),
 - Infection,
 - Absolute neutrophil count (ANC) nadir,
 - Duration of severe neutropenia (DSN).
- The search engines were NCBI, PubMed, and Google Scholar databases.
- As outlined in the PRISMA diagram below, 36 studies remained for our correlative analyses, representing a total number of **7314** patients.



- To evaluate the validity of the dataset, we first established that correlations between the historically accepted Chemotherapy Induced Neutropenia endpoints Febrile Neutropenia (FN) rate, duration of severe neutropenia (DSN), and absolute neutrophil count nadir were significant, which was the case (data presented in poster 2021 ESMO #3574)
- Next, we correlated Gr4N frequency with FN rate, DSN, absolute neutrophil count Nadir, Hospitalization rate, and Infection rate (see under Results)
- Based on these correlations we calculated the CIN outcomes (FN rate, DSN, Hospitalization rate, ANC Nadir, Infection rate) for the two scenarios of Gr4N of 86% and Gr4N of 68%.

RESULTS

- Best Fit Correlations between Gr4N frequency and CIN outcomes shown below
 - The left dotted line represents the 68% Gr4N frequency as was observed with the Plinabulin/Pegfilgrastim combination, and the right dotted line represents the 86% Gr4N frequency as was observed with Pegfilgrastim alone in PROTECTIVE-2



- Clinical Outcomes for CIN with a Gr4N of 86% vs 68% are summarized below.

Grade 4 Neutropenia Frequency	Mean DSN	FN rate	Hospitalization rate	Mean ANC nadir	Infection rate
86% (Peg Alone)	3.01	24.3	20.6	0.197	16.5
68% (Plin+Peg)	1.66	10.1	8.29	0.395	8.17
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

DSN- Duration of severe neutropenia, FN-Febrile neutropenia, ANC-Absolute neutrophil count

CONCLUSIONS

- A reduction of Grade 4 Neutropenia (Gr4N) frequency from 86% to 68% by adding Plinabulin to Pegfilgrastim in an ‘All Chemotherapy and All Cancers’ setting is predicted to be not only statistically, but also clinically highly significant.**

DISCLOSURE

Disclosures: The first author has no actual or potential conflict of interest in this program.
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Study Sponsored by:

