

# ESMO # 3574 : Severe Neutropenia (Grade 4 Neutropenia) as a Population-Based Predictor for Adverse Clinical Outcome of Chemotherapy Induced Neutropenia

R. Mohanlal<sup>1</sup>, S. Ogenstad<sup>2</sup>, G. Lyman<sup>3</sup>, L. Huang<sup>1</sup>, D. Blayne<sup>4</sup>

<sup>1</sup>Clinical Research & Development, BeyondSpring Pharmaceuticals, New York, United States of America, <sup>2</sup>Statogen Consulting LLC, 7501 Hasentree Way, North Carolina, United States of America, <sup>3</sup>Fred Hutchinson Cancer Research Center, Washington, <sup>4</sup>Medicine - Oncology, Stanford University, Stanford, CA, United States of America

## BACKGROUND

- Chemotherapy Induced Neutropenia (CIN) is a frequently occurring side effect in cancer patients receiving myelosuppressive chemotherapy
- Current CIN risk assessment is based on Febrile Neutropenia (FN) frequency, which requires input on the two variables Absolute Neutrophil Count (ANC) and Fever
- An alternative endpoint of duration of severe neutropenia (DSN) is also used for CIN risk assessment, but requires almost daily blood draws for ANC to be reliable, thus not practical
- In the COVID-era, a simplified risk assessment algorithm for CIN might enable optimizing resource utilization, since CIN with fever triggers ER/Hospital visits
- Grade 4 Neutropenia (Gr4N) frequency** is generally well-characterized for all chemotherapies and clinical settings and can be reliably obtained through a **single** ANC blood draw around the time of ANC nadir (which is well-established for all chemotherapies)
- Gr4N frequency might represent a reliable and simple-to-use CIN risk assessment tool, which is validated in this study

## 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

- To evaluate the validity of the dataset, we first evaluated correlations between the historically accepted CIN endpoints FN rate, DSN and Absolute Neutrophil Count (ANC) Nadir.

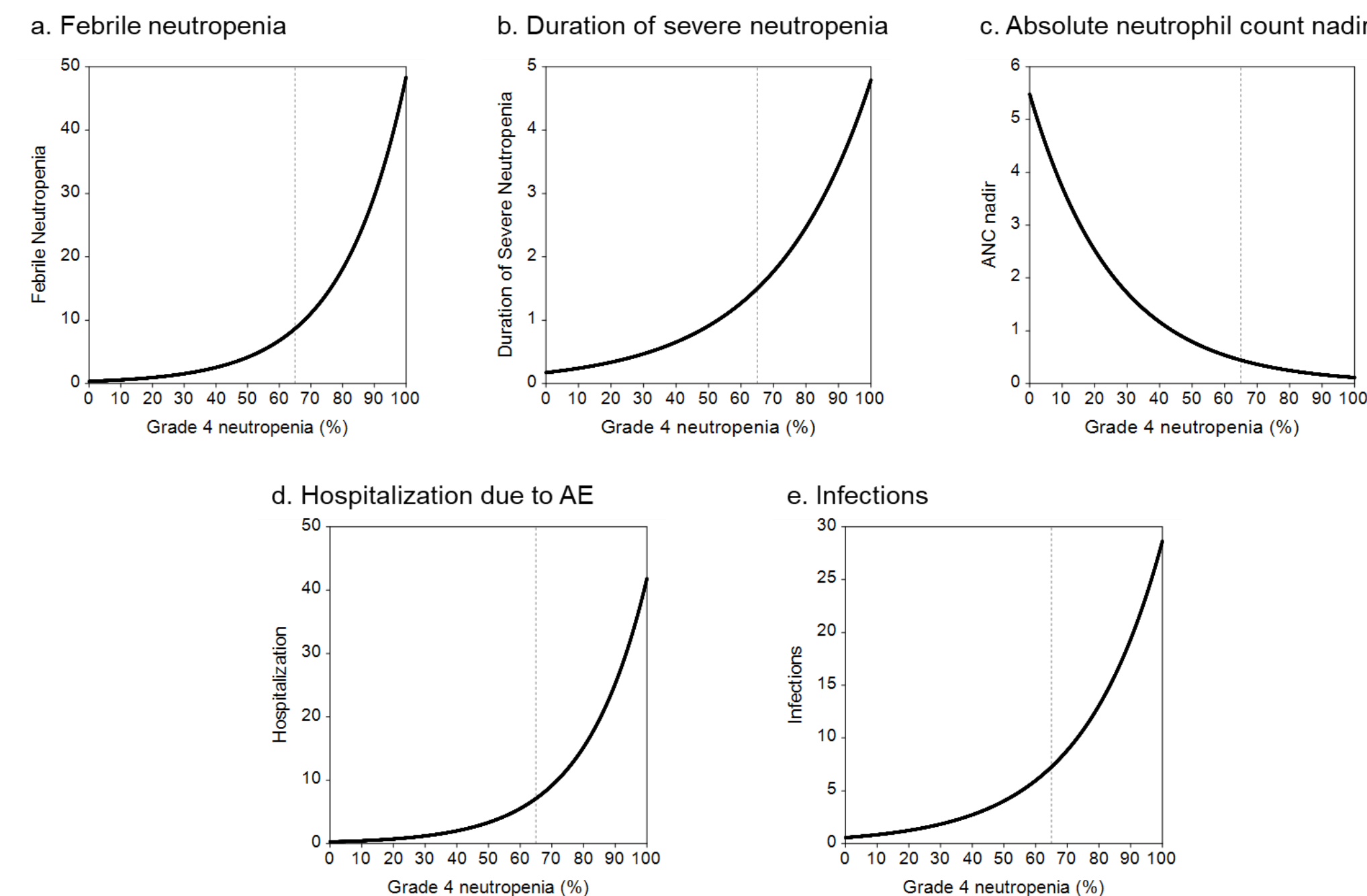
- Next, we correlated Gr4N frequency with FN rate, DSN, ANC Nadir, Hospitalization rate, and Infection rate.

## RESULTS

- Correlation between accepted endpoints for CIN risk assessment (FN, DSN, ANC Nadir) were strong and statistically significant, thereby confirming the validity of the meta-analysis dataset.

	DSN	ANC Nadir
FN	Pseudo R=0.73; p<0.0001; N=7477	Pseudo R=-0.76; p<0.0001; N=4994
DSN		Pseudo R=-0.91; p<0.0001; N=5325

- Best fit curves between Gr4N and CIN outcomes (FN, DSN, ANC Nadir, Hospitalization Rate, Infection Rate) is shown in the graphs below, and summary statistics in the table below



- Grade 4 Neutropenia (Gr4N) Frequency showed a strong correlation with FN, DSN, ANC Nadir, Hospitalization Rate, Infection Rate

	FN Rate	DSN	ANC Nadir	Hospitalization Rate	Infection Rate
Gr4N Frequency	Pseudo R=0.44 n=4311 P<0.0001	Pseudo R=0.65 N=4864 P<0.0001	Pseudo R=-0.77 N=2623 P<0.0001	Pseudo R=0.69 N=850 P<0.0001	Pseudo R=0.43 N=2042 P<0.0001

- The Gr4N threshold of 65% depicted the separation of Low versus High CIN Risk based on meeting these two criteria:

- DSN of <1 day (considered to be not clinically significant)
- FN risk <10% (as defined by NCCN)

- For all CIN Risk variables (except ANC Nadir), the curve was relatively flat between Gr4N 0% - 65%, with an exponential rise with Gr4N of 65% or higher

- For ANC Nadir, the curve was relatively flat for Gr4N ≥ 65% as to be expected

- The Gr4N threshold of 65% depicted the separation between Low versus High CIN Risk.

	Grade 4 Neutropenia <65% Mean (95%CI), N	Grade 4 Neutropenia ≥65% Mean (95%CI), N	P-value
DSN	0.99 (0.97, 1.013), 2659	2.14 (2.084, 2.19), 2205	<0.0001
FN rate	4.50 (4.32, 4.68), 2659	11.78 (11.30, 12.26), 1652	<0.0001
ANC nadir	1.11 (1.082, 1.15), 1586	0.33 (0.31, 0.35), 1037	<0.0001
Hospitalization rate	4.17 (3.70, 4.63), 435	15.93 (15.16, 16.70), 415	<0.0001
Infection rate	4.38 (4.10, 4.66), 806	11.41 (10.39, 12.43), 1236	<0.0001

DSN-duration of Severe Neutropenia, FN-febrile neutropenia, NC-Absolute neutropenia count

## CONCLUSIONS

- Grade 4 Neutropenia (Gr4N) frequency is a valid, binary and easy-to-use predictor of CIN outcomes
- The 65% Gr4N frequency threshold depicts Low vs. High CIN outcome risk.

## DISCLOSURE

Disclosures: The first author discloses employment, leadership and stocks interests in BeyondSpring Pharmaceuticals Inc.

Corresponding Author: Ramon Mohanlal, MD, PhD - [rmohanlal@beyondspringpharma.com](mailto:rmohanlal@beyondspringpharma.com)

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