(MPN-1218) RUXOLITINIB AND INTERFERON ALFA INDUCE SUPERIOR RATES OF COMPLETE PERIPHERAL BLOOD COUNT REMISSION COMPARED TO ANAGRELIDE IN HYDROXYUREA-EXPOSED ESSENTIAL THROMBOCYTHEMIA

T. VITHALA[1], S. LEE[2], H. ROBERTS[1], S. HANDA[1], J. VAUGHN[1], S. WALL[1], P. ZHANG[2], **A. SRISUWANANUKORN[1]**

[1]The Ohio State University College of Medicine, Columbus, OH, United States

[2]The Ohio State University College of Engineering, Columbus, OH, United States

The James

The Ohio State University Comprehensive Cancer Center

Introduction

Essential thrombocythemia (ET) is a myeloproliferative neoplasm (MPN) characterized by elevated platelets and a predilection for thrombotic events.

Hydroxyurea (HU) is a commonly prescribed front-line therapy to achieve a reduction of platelet (PLT) and white blood cell (WBC) counts.

The optimal **2nd-line therapy** in ET patients intolerable or resistant to HU is largely unknown.

Objective

To compare **complete peripheral blood count remission (CPBCR)** in **HU-exposed ET patients** between the commonly prescribed 2nd-line agents including:

- Anagrelide (ANA)
- Busulfan (BUS)
- Ruxolitinib (RUX)
- Interferon Alfa (IFN)—comprised of both Peginterferon Alfa-2a (PEG) and Ropeginterferon Alfa-2b-njft (ROPEG)

Methods

Data: Epic Cosmos Database - a single vendor database of more than 299 million patients and 15.5 billion encounters

Cohort: ET patients defined by ICD-10 code and PLT count ≥ 450 x 10^9/L treated between December 2010 - December 2024

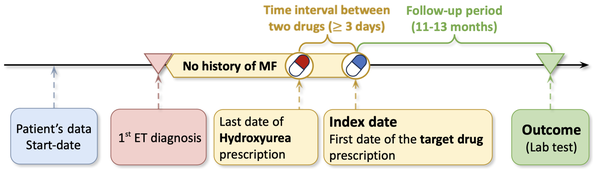


Figure 1: Schema for Patient Identification

Endpoint: CPBCR after 12 ± 1 months of 2nd-line therapy.

- PLT ≤ 400 x 10^9/L
- WBC ≤ 10 x 10^9/L

Note: Spleen volume/length is NOT available.

Analysis: logistic regression after propensity score matching for age, sex, race, and baseline PLT and WBC count

Patient Cohort

	ANA	BUS	PEG	ROPEG	RUX
# Patients	228	69	101	35	315
Age	73.0 (67, 83)	62.0 (37, 73)	61.0 (44, 72)	61.0 (51, 68)	73.0 (64, 80)
Sex, Female	139 (61.0%)	39 (56.5%)	63 (62.4%)	22 (62.9%)	177 (56.2%)
Race, Caucasian	178 (78.1%)	50 (72.5%)	80 (79.2%)	28 (80.0%)	269 (85.4%)
PLT (x 10^9/L) at Baseline	689 (527, 902)	411 (182, 778)	656 (473, 987)	515 (411, 724)	530 (341, 772)
WBC (x 10^9/L) at Baseline	7.7 (5.7, 10.3)	7.4 (5.0, 12.5)	7.5 (5.4, 11.9)	7.2 (5.6, 10.0)	9.3 (6.2, 14.0)

Table 1: Demographics of Patient Population

Results

	ANA	BUS	PEG	ROPEG	RUX
# Patients	228	69	101	35	315
PLT @ 12mo	449.0 (318.8, 605.2)	261.0 (137.0, 408.0)	403.0 (301.0, 521.0)	376.0 (275.0, 434.5)	390.0 (264.0, 521.0)
PLT Reduction	-218.0 (-402.0, -12.8)	-98.0 (-420.0, 0.0)	-262.0 (-534.0, -44.0)	-171.0 (-351.0, -31.0)	-130.0 (-316.5, 37.0)
WBC @ 12mo	9.9 (7.4, 12.5)	6.0 (4.4, 8.3)	5.2 (4.0, 8.3)	5.0 (4.0, 6.7)	8.2 (6.0, 11.8)
WBC Reduction	1.5 (-0.5, 4.9)	-1.5 (-5.5, 1.2)	-2.1 (-5.1, 0.6)	-2.1 (-3.9, -0.3)	-0.7 (-3.8, 2.2)
Achieved CPBCR	46 (20.2%)	46 (66.7%)	47 (46.5%)	19 (54.3%)	112 (35.6%)
MF within 2 years	15 (6.6%)	6 (8.7%)	5 (5.0%)	2 (5.7%)	81 (25.7%)**

Table 2: Results of 2nd-line Therapies in ET. **Ongoing quality control to define transformation of ET to MF

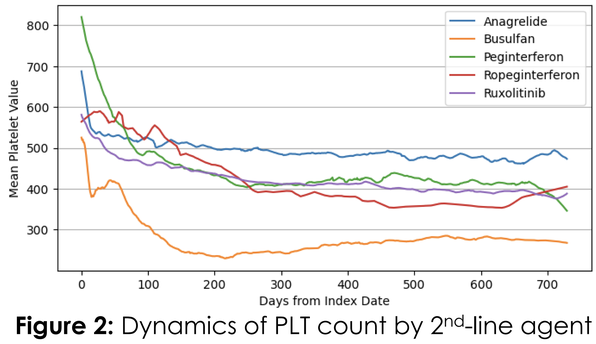


Figure 2: Dynamics of PLT count by 2nd-line agent

Case	Control	# Case	# Control	HR w/ PSM	p
ANA	BUS	274	83	2.08	0.002
ANA	IFN	267	164	1.68	0.000
ANA	RUX	248	346	1.35	0.005
BUS	IFN	86	174	0.80	0.359
BUS	RUX	74	355	0.47	0.003
IFN	RUX	157	340	0.68**	0.010

Table 3: Pairwise comparison 2nd-line Therapies in ET. Propensity Score Matching (PSM) as per methods. HR > 1 suggest Case is inferior in achieving CPBCR. **Ongoing quality control to define MF population and truly assess if IFN superior to RUX

Summary

- Though off-label, **RUX appears to be commonly utilized** as a 2nd-line therapy
- In pairwise comparisons, **RUX and IFN were both superior to ANA** for CPBCR
- **IFN** led to the **highest degree of platelet response**
- Though technically superior for CPBCR, likely adverse profile (not currently analyzed) lead to **lower utilization of BUS**

Discussion

- Though ANA is a commonly used 2nd-line agent, our results suggest alternative superior agents
- Our findings are in-line with the recently announced prospective **SURPASS-ET** trial, revealing **superiority of ROPEG over ANA**
- **Ongoing analysis** for thrombotic events and transformation to myelofibrosis/leukemia

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sris01@osumc.edu

@andrewsris1

The Ohio State University