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– ORIGINAL PAPERS –

Evaluation of the Benefit of Ropeginterferon Treatment in Patients with Polycythemia Vera

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Abstract

Results: Twenty-three patients (15 men and 8 women) with a median age of 57 years were enrolled, with 87.5% having the JAK617F mutation. Six patients had a history of thrombosis. Besremi was used as a first-line treatment in 11 patients and as a second-line treatment in 12 patients after Hydroxyurea administration. Complete hematologic response, defined by normalized blood counts and symptom resolution, was achieved in 3.46 ± 2.53 months in more than 50% of patients. One patient discontinued treatment, two did not achieve complete response, and four had less than 3 months of follow-up. After 6 months, the mean hematocrit was 44.17 ± 7.76 ($p = 0.01$), WBC $7.6 \pm 3.92 \times 1000/mm^3$ ($p = 0.02$), and thrombocytosis significantly decreased in the first month ($p = 0.02$).

Conclusions: Ropeginterferon treatment improved the quality of life for all patients, eliminating symptoms of cardiovascular and thrombotic complications. Approximately 60% of patients achieved complete hematologic response within the first 3 months.

Keywords: polycythemia vera, myeloproliferative neoplasm, Ropeginterferon, treatment

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Introduction

Polycythemia vera (PV) is a chronic myeloproliferative neoplasm (MPN) characterized by the overproduction of red blood cells, often associated with elevated white blood cells and platelets due to the clonal proliferation of hematopoietic stem cells. It is frequently linked to mutations in the JAK2 gene, most commonly the JAK2 V617F mutation, which is present in more than 90% of patients diagnosed with PV. JAK2 mutation, whose main role is represented by activating the JAK-STAT signalling

pathway, increases the thrombotic risk when acquired. Some studies highlight the presence of said-mutation even before the onset of symptoms, with long-term haematological implications and modifications before the official diagnosis of PV [1,2].

Pancytosis increases the blood viscosity which causes a series of microcirculatory disorders and a further increase in thrombotic risk. The important blood viscosity in patients diagnosed with polycythemia vera is not the effect of solely polyglobulia, but also of the changes in

erythrocytes deformability, aggregation, adhesion proteins expression, elevated phosphatidylserine expression and microvesicles release [1,3-5].

PV, like other myeloproliferative neoplasms, can lead to various complications, with the most common being thrombotic events and splenomegaly. Additionally, a percentage of individuals with PV are at an increased risk of progression to secondary myelofibrosis or acute myeloid leukemia. Numerous factors such as age above 60 years old, history of thrombosis, phlebotomies as sole treatment, alongside the cardiovascular factors (hypertension, diabetes mellitus, dyslipidemia) increase the thrombotic risk [3-5].

The management of polycythemia vera primarily focuses on improving quality of life and reducing the risk of complications. Treatment strategies include phlebotomy, the use of low-dose aspirin, and cytoreductive therapies such as Hydroxyurea, Interferon-alpha, and Ruxolitinib [1,6-9].

Besremi (Ropeginterferon alfa-2b) is a long-acting interferon used in the treatment of PV. Its prolonged half-life is attributed to the attachment of a polyethylene glycol (PEG) molecule to interferon alpha, which allows for less frequent dosing compared to standard interferons [6-9].

The safety profile is relatively favorable, with most frequent adverse effects being hematological (represented by leukopenia and thrombocytopenia, followed by anaemia). Other important adverse effects observed in a high percentage of population under Besremi were: hepatotoxicity, thyroid toxicity, myalgia, viral infection-like symptoms, pruritus, diarrhoea, headache and local reactions at the site of injection [6-9].

Material and methods

We performed an observational retrospective study using patient data acquired from Colentina Clinical Hospital, Department of Hematology I, between 2022 and 2024. A total of 23 patients (both males and females), aged between 45 and 75 years, were identified. The main objective was the evaluation of the benefit of Ropeginterferon treatment in PV patients. The secondary objective was the evaluation of adverse events and the symptomatology resolution/amelioration.

To be included in the study, patients had to meet the following criteria:

1. A primary diagnosis of polycythemia vera (PV);
2. In treatment with Besremi (Ropeginterferon alfa-2b);
3. Treatment adherence;
4. Informed consent;

Four exclusion criteria were implemented in order to ensure more accurate data:

1. A diagnosis other than polycythemia vera,
2. Uncertainty regarding treatment adherence,
3. Lack of complete blood records
4. Insufficient patient history data.

The database included the following patient information: initials, age, sex, presence or absence of the JAK2 V617F mutation, initial treatment, comorbidities, CBC data at baseline (start of treatment), and at 1 month, 3 months, 6 months and 1 year after initiation of Besremi. Additionally, the database recorded the current dose of Ropeginterferon and any complications encountered.

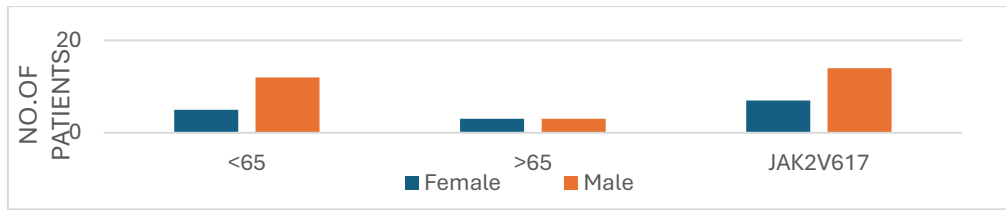
The statistical analyses were performed using MedCalc Statistical Software version 23.0.9 (MedCalc Software Ltd, Ostend, Belgium). In order to test for "Normal distribution of variables", the statistical software allowed us to use the D'Agostino-Pearson test. As a result to the normal distribution of all analysed variables, the statistical analysis of all variables was done using parametric tests: Anova one way analysis of variance test. Obtained results were expressed using mean value and standard deviation, with a statistically significant P value of less or equal than 0.5.

The correlation between variables was performed with the aid of correlation-coefficient test, with a P value of less or equal than 0.5 for it being considered statistically significant.

Results

This retrospective study is composed of 23 patients, 15 males and 8 females, with a median age of 57 years old, 87.5% having the JAK617F mutation.

Besremi was used as a first-line treatment in 10 patients, while the remaining 13 patients received Besremi (Ropeginterferon alfa-2b) as second-line therapy after prior treatment with Hydroxyurea.



Graphic 1. The incidence of males and females regarding age and presence of JAK2 V617F mutation

The main objective of this study was to determine the benefits of Besremi in patients with polycythemia vera. In order to achieve this, we examined the evolution of complete blood count (CBC) parameters at different time points: baseline, 1 month, 3 months, and 6 months after

the initiation of treatment. Additionally, we have analysed the data by separating the individuals into two separate subgroups. The group A has received Besremi as first-line, while group B started Besremi treatment as a second-line option.

	N	Minimum	Maximum	Mean	Median	SD	RSD	SEM	25 - 75 P
HB1	8	12,700	20,100	16,687	16,400	2,1931	0,1314	0,7754	15,800 to 18,150
HB2	7	13,100	17,900	15,500	15,400	1,4742	0,09511	0,5572	15,000 to 16,275
HB3	6	13,300	18,900	15,517	15,350	1,9580	0,1262	0,7993	14,100 to 16,100
HB4	4	12,000	17,500	15,175	15,600	2,7281	0,1798	1,3640	12,900 to 17,450
HB5	2	13,000	13,800	13,400	13,400	0,5657	0,04222	0,4000	13,000 to 13,800
HT1	8	40,020	61,800	51,585	51,080	7,0911	0,1375	2,5071	47,450 to 56,900
HT2	7	42,200	53,500	47,986	47,900	3,7654	0,07847	1,4232	45,975 to 50,850
HT3	6	41,600	50,000	45,600	45,450	3,1119	0,06824	1,2704	43,000 to 48,100
HT4	4	39,300	54,600	47,175	47,400	7,6973	0,1632	3,8487	40,600 to 53,750
HT5	2	39,800	41,300	40,550	40,550	1,0607	0,02616	0,7500	39,800 to 41,300
LDH1	8	186,000	26100,000	3466,125	228,500	9145,5526	2,6386	3233,4411	203,000 to 290,000
LDH2	4	171,000	235,000	201,750	200,500	27,2932	0,1353	13,6466	181,000 to 222,500
LDH3	3	195,000	198,000	196,333	196,000	1,5275	0,007780	0,8819	195,250 to 197,500
LDH4	4	140,000	338,000	226,500	214,000	82,3104	0,3634	41,1552	173,500 to 279,500
LDH5	1	195,000	195,000	195,000	195,000				195,000 to 195,000
LYM1	7	830,000	2790,000	1794,286	1820,000	682,6629	0,3805	258,0223	1212,500 to 2212,500
LYM2	7	1210,000	2490,000	1855,714	1900,000	411,1714	0,2216	155,4082	1585,000 to 2047,500
LYM3	6	970,000	1780,000	1481,667	1535,000	301,5571	0,2035	123,1102	1320,000 to 1750,000
LYM4	4	850,000	1930,000	1382,500	1375,000	603,7315	0,4367	301,8657	860,000 to 1905,000
LYM5	2	1020,000	1300,000	1160,000	1160,000	197,9899	0,1707	140,0000	1020,000 to 1300,000
NE1	8	3790,000	14530,000	6227,500	4650,000	3823,6996	0,6140	1351,8820	3850,000 to 7250,000
NE2	7	2570,000	12700,000	6804,286	6170,000	4040,8698	0,5939	1527,3052	3370,000 to 10542,500
NE3	6	2070,000	7230,000	5703,333	6185,000	1855,9490	0,3254	757,6880	5750,000 to 6800,000
NE4	4	2690,000	6720,000	4562,500	4420,000	1943,0796	0,4259	971,5398	2930,000 to 6195,000
NE5	2	2150,000	4530,000	3340,000	3340,000	1682,9141	0,5039	1190,0000	2150,000 to 4530,000
NLR1	7	1,630	8,550	4,111	3,610	2,5290	0,6151	0,9559	1,937 to 5,585
NLR2	7	1,320	9,480	4,051	4,080	2,9743	0,7341	1,1242	1,552 to 5,617
NLR3	6	1,160	7,010	4,125	4,105	1,8700	0,4533	0,7634	3,760 to 4,610
NLR4	4	1,394	7,906	4,376	4,102	3,3253	0,7599	1,6627	1,540 to 7,212
NLR5	2	1,654	4,441	3,048	3,048	1,9709	0,6467	1,3937	1,654 to 4,441
PLT1	8	189000,000	903000,000	497750,000	480000,000	253610,9225	0,5095	89665,0015	281000,000 to 684000,000
PLT2	7	247000,000	687000,000	493714,286	575000,000	194957,8709	0,3949	73687,1489	291500,000 to 667250,000
PLT3	6	140000,000	656000,000	480500,000	569500,000	194061,5882	0,4039	79225,3116	362000,000 to 586000,000
PLT4	4	179000,000	416000,000	327250,000	357000,000	105553,6988	0,3225	52776,8494	253000,000 to 401500,000
PLT5	2	222000,000	226000,000	224000,000	224000,000	2828,4271	0,01263	2000,0000	222000,000 to 226000,000
WBC1	8	5550,000	17670,000	8800,000	7660,000	4134,1366	0,4698	1461,6380	5790,000 to 10140,000
WBC2	7	5140,000	16030,000	9500,000	8630,000	4026,2638	0,4238	1521,7847	6145,000 to 12615,000
WBC3	6	4550,000	10120,000	8045,000	8435,000	1847,3413	0,2296	754,1739	8240,000 to 8490,000
WBC4	4	5450,000	8790,000	6790,000	6460,000	1492,8943	0,2199	746,4471	5665,000 to 7915,000
WBC5	2	4010,000	6550,000	5280,000	5280,000	1796,0512	0,3402	1270,0000	4010,000 to 6550,000

Picture 1. Statistical analysis of Group A's complete blood count values; the number of patients (N), minimum value, maximum value, mean value, median, standard deviation (SD), relative standard deviation (RSD), standard error of the mean (SEM) for the Hemoglobin (HB), Hematocrit (HT), Lactate dehydrogenase (LDH), Lymphocytes (LYM),

Neutrophils (NE), Platelets (PLT), White blood count (WBC) at baseline (1), after one month (2), three months (3), 6 months (4) and one year (5) of treatment with Besremi.

	N	Minimum	Maximum	Mean	Median	SD	RSD	SEM	25 - 75 P
HB1	15	10,100	21,400	16,253	16,400	2,3546	0,1449	0,6080	15,025 to 17,175
HB2	15	9,400	21,100	16,233	16,400	2,5278	0,1557	0,6527	15,825 to 17,200
HB3	13	10,000	18,700	15,215	15,200	2,4279	0,1596	0,6734	13,550 to 16,525
HB4	7	10,100	17,200	14,714	15,200	2,4498	0,1665	0,9259	13,450 to 16,375
HB5	3	9,000	16,000	12,667	13,000	3,5119	0,2773	2,0276	10,000 to 15,250
HT1	15	37,400	61,900	49,000	49,000	6,1744	0,1260	1,5942	45,600 to 53,100
HT2	15	35,500	58,300	49,300	48,800	5,6916	0,1154	1,4696	46,400 to 53,575
HT3	13	36,700	58,500	45,823	46,400	6,4941	0,1417	1,8011	39,150 to 50,825
HT4	7	37,300	51,900	44,486	45,400	5,5186	0,1241	2,0858	39,050 to 48,550
HT5	3	33,100	53,900	41,433	37,300	10,9988	0,2655	6,3502	34,150 to 49,750
LDH1	14	167,000	365,000	254,714	244,500	55,5967	0,2183	14,8588	221,000 to 302,000
LDH2	13	145,000	484,000	258,923	241,000	86,9775	0,3359	24,1232	203,750 to 279,500
LDH3	9	146,000	358,000	249,333	242,000	74,5587	0,2990	24,8529	198,250 to 306,000
LDH4	7	161,000	392,000	252,429	241,000	86,0423	0,3409	32,5210	175,000 to 316,250
LDH5	2	157,000	340,000	248,500	248,500	129,4005	0,5207	91,5000	157,000 to 340,000
LYM1	15	1040,000	4970,000	2157,333	1870,000	1209,4832	0,5606	312,2872	1520,000 to 1990,000
LYM2	15	640,000	5240,000	2042,667	1770,000	1101,1777	0,5391	284,3229	1615,000 to 2052,500
LYM3	13	810,000	3460,000	1732,308	1580,000	698,5002	0,4032	193,7291	1282,500 to 1940,000
LYM4	7	1040,000	2870,000	1547,143	1430,000	625,4522	0,4043	236,3987	1132,500 to 1635,000
LYM5	3	1160,000	2080,000	1676,667	1790,000	470,3545	0,2805	271,5593	1317,500 to 2007,500
NE1	15	3110,000	40410,000	8775,333	6210,000	9243,8581	1,0534	2386,7539	4305,000 to 8390,000
NE2	15	2280,000	23660,000	6894,000	5620,000	5349,4243	0,7760	1381,2154	3252,500 to 8125,000
NE3	13	1990,000	22340,000	6075,385	4930,000	5421,7504	0,8924	1503,7230	2735,000 to 6475,000
NE4	7	2200,000	16650,000	5860,000	3360,000	5090,6090	0,8687	1924,0693	2672,500 to 6745,000
NE5	3	1530,000	15230,000	8153,333	7700,000	6861,2414	0,8415	3961,3396	3072,500 to 13347,500
NLR1	15	1,020	13,930	4,251	3,730	3,1399	0,7387	0,8107	2,155 to 4,395
NLR2	15	0,780	10,800	3,762	3,430	2,5400	0,6752	0,6558	2,030 to 5,032
NLR3	13	0,790	8,300	3,528	3,320	2,1080	0,5976	0,5847	1,805 to 4,890
NLR4	7	1,528	5,865	3,529	3,083	1,7912	0,5076	0,6770	1,946 to 5,375
NLR5	3	1,319	7,322	4,314	4,302	3,0016	0,6957	1,7330	2,065 to 6,567
PLT1	15	155000,000	1207000,000	482533,333	371000,000	290054,1493	0,6011	74891,6593	250000,000 to 639500,000
PLT2	15	107000,000	708000,000	423866,667	463000,000	186195,3148	0,4393	48075,4235	255000,000 to 542750,000
PLT3	13	107000,000	676000,000	367384,615	399000,000	182118,7975	0,4957	50510,6664	183250,000 to 476500,000
PLT4	7	75000,000	439000,000	280714,286	324000,000	143786,5481	0,5122	54346,2069	156750,000 to 402000,000
PLT5	3	133000,000	406000,000	284000,000	313000,000	138791,2101	0,4887	80131,1425	178000,000 to 382750,000
WBC1	15	4980,000	46460,000	11952,000	8860,000	10252,3462	0,8578	2647,1444	6670,000 to 14267,500
WBC2	15	3500,000	27870,000	9836,000	10080,000	5873,6029	0,5972	1516,5578	6122,500 to 10955,000
WBC3	13	3580,000	27540,000	8751,538	7650,000	6250,1585	0,7142	1733,4821	4920,000 to 9235,000
WBC4	7	4020,000	21540,000	8261,429	5370,000	6155,9576	0,7451	2326,7333	4730,000 to 8955,000
WBC5	3	2970,000	19210,000	10796,667	10210,000	8135,8794	0,7536	4697,2522	4780,000 to 16960,000

Picture 2. Statistical analysis of Group B's complete blood count values; the number of patients (N), minimum value, maximum value, mean value, median, standard deviation (SD), relative standard deviation (RSD), standard error of the mean (SEM) for the Hemoglobin (HB), Hematocrit (HT), Lactate dehydrogenase (LDH), Lymphocytes (LYM), Neutrophils (NE), Platelets (PLT), White blood count (WBC) at baseline (1), after one month (2), three months (3), 6 months (4) and one year (5) of treatment with Besremi

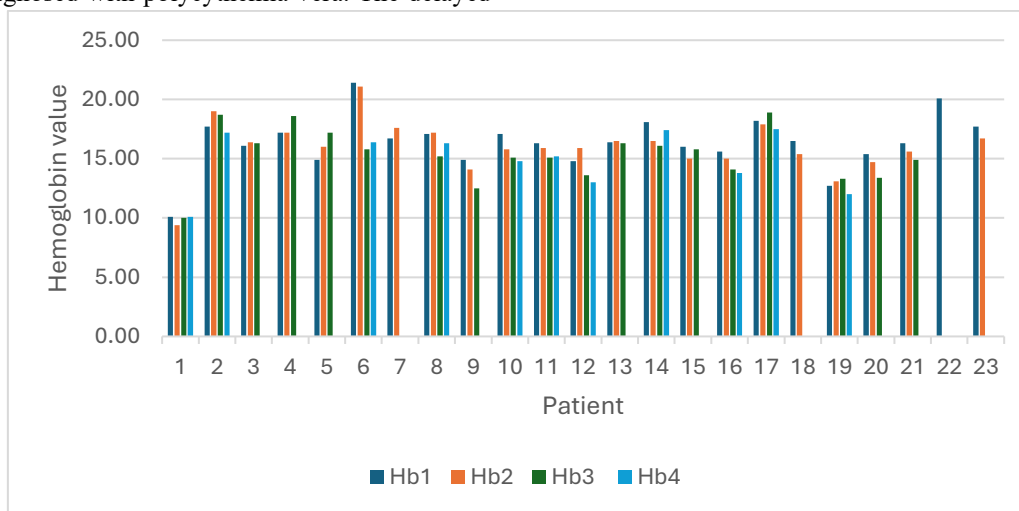
Regarding hemoglobin levels, for the general cohort we observed a slight decrease in the mean value over the 6-month period. At baseline, the mean hemoglobin was 16.40 with a standard deviation of 2.21. After 6 months of treatment, the mean value decreased to 15.08 with a standard deviation of 2.11. The relatively stable standard deviation suggests that there was consistent variability in

hemoglobin levels among the patients over time, despite the slight decrease in the mean.

Group A had rapid and substantial decrease in hemoglobin levels (with a mean value decreasing from 16.687 to 15.500), while group B demonstrated a delayed response, with hemoglobin levels remaining above normal for the first 3 months of treatment, before eventually decreasing.

This data shows the great efficacy of Besremi in controlling hemoglobin levels as first-line treatment for patients diagnosed with polycythemia vera. The delayed

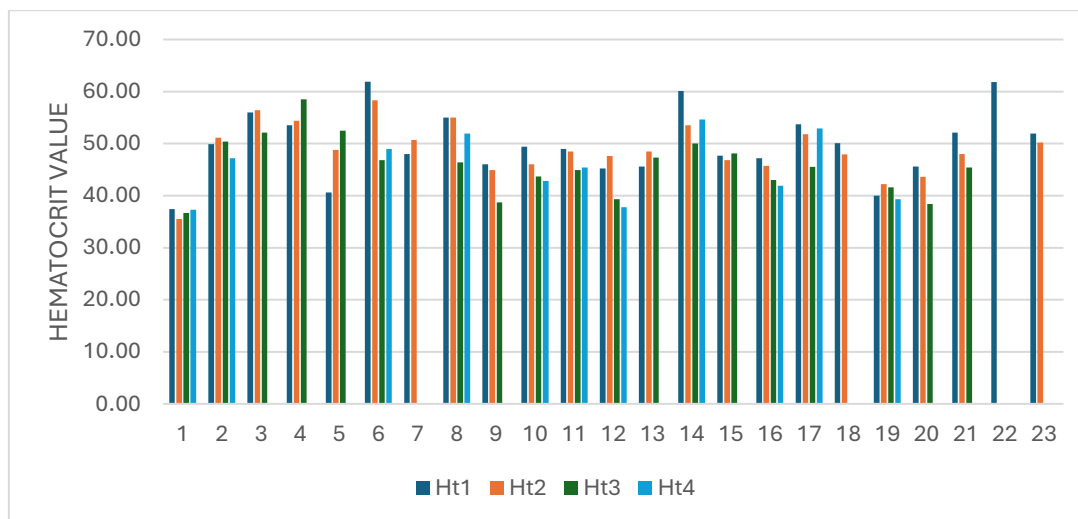
response in the patients primarily treated with Hydroxyurea should be further investigated.



Graphic 2: The hemoglobin (HB) evolution at baseline (1) and 1 months (2), 3 months (3) and 6 months (4) after the initiation of treatment

When analyzing hematocrit levels, Group A demonstrates an immediate response, with the mean value decreasing from 51.585 to 47.986 within the first month. After the first 3 months of treatment, we can observe a mean value of 45.600, which further highlights the favorable response to Besremi when used as a first-line treatment option.

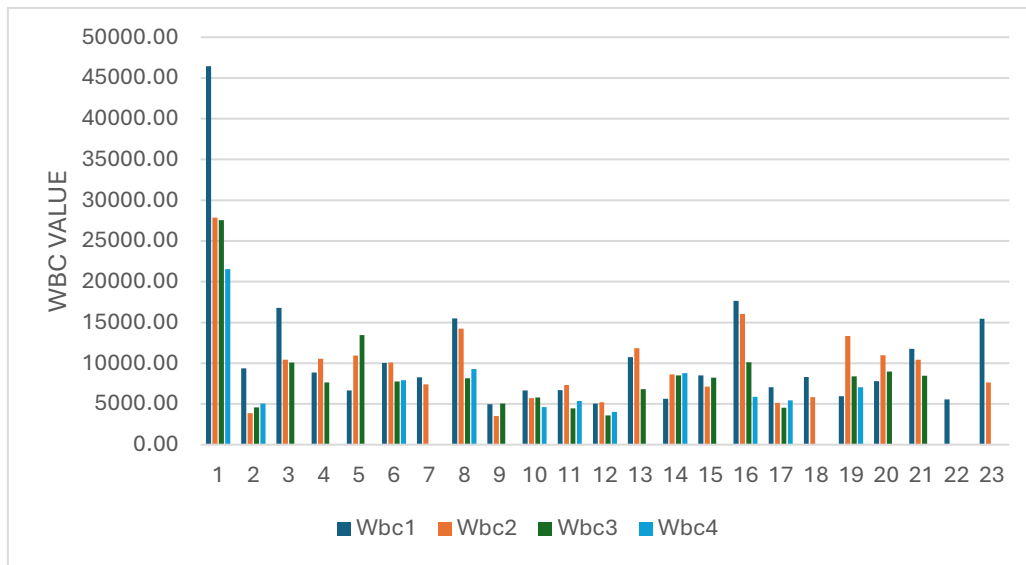
In contrast, Group B shows a delayed response, emphasising the slow-acting effect when used as a second-line treatment option (after the first month, the mean value was approximately equal to the value at baseline, with a substantial decrease after 3 months).



Graphic 3: The hematocrit (HT) evolution at baseline (1) and 1 months (2), 3 months (3) and 6 months (4) after the initiation of treatment

When comparing the two subgroups, the white blood cell (WBC) levels at baseline are initially higher in patients from Group B but normalize after 3 months of treatment. Additionally, the wide range of WBC levels in Group B at

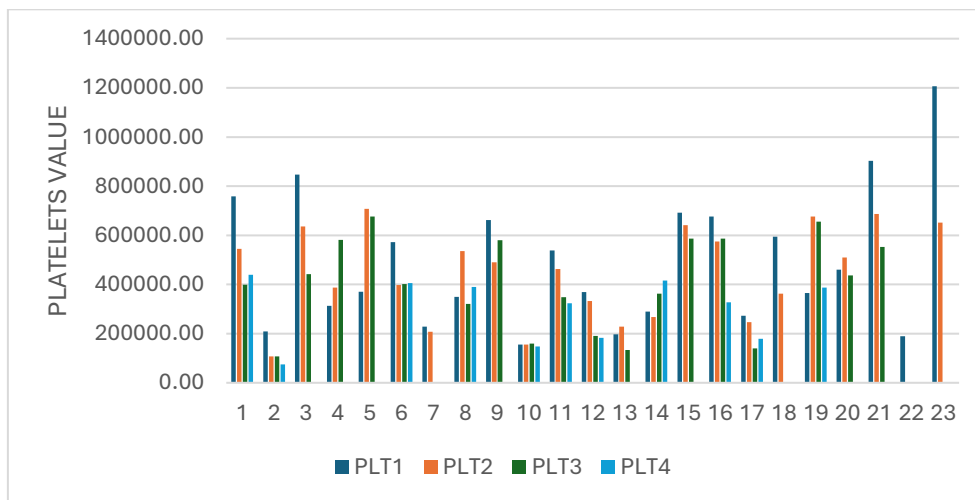
baseline highlights the significant variability between the maximum and minimum values. This could be attributed to differing responses to Hydroxyurea prior to the initiation of Besremi.



Graphic 4: The white blood cells (WBC) evolution at baseline (1) and 1 months (2), 3 months (3) and 6 months (4) after the initiation of treatment

The platelet analysis reveals that Group A has higher overall values, with a substantial decrease observed over

time. In contrast, Group B exhibits a less pronounced but still meaningful decline in platelet levels.



Graphic 5: The platelets (PLT) evolution at baseline (1) and 1 months (2), 3 months (3) and 6 months (4) after the initiation of treatment

The study also noted the management of symptoms such as fatigue, headaches, pruritus, excessive night sweats, and symptoms related to splenomegaly and/or thrombosis. Complete resolution of symptoms was observed in 11 patients, while 3 patients experienced partial improvement. Three patients discontinued treatment, 3 patients continued to report fatigue and/or

significant splenomegaly with no substantial improvement, and 4 patients had been undergoing treatment for less than 3 months at the time of reporting. Additionally, we have observed the adverse effects of Besremi in our cohort.

In two patients, we had to discontinue treatment as a result of the hepatotoxicity expressed as an important elevation

in serum glutamic oxaloacetic transaminase (GOT) and serum glutamic pyruvic transaminase (GPT). The dose of one patient, included in group A, was reduced from 250 μg to 150 μg after 5 months of treatment. After normalization of GOT and GPT, the dose was upgraded and maintained to 200 μg with no more evidence of hepatotoxicity at the present time. The other patient, included in group B, was switched to a third-line treatment option, Ruxolitinib (Jakafi) with a favorable evolution.

One other patient was switched to Ruxolitinib after approximately 1 year of treatment due to secondary anemia (Hb = 9g/dL) associated with leukocytosis and neutrofilia. Lastly, we had to reintroduce Hydroxyurea to one individual, as he was not achieving complete hematological response to Besremi alone. Both patients were in group B, with prior utilization of Hydroxyurea.

Discussions

This retrospective study aims to illustrate the efficiency of Besremi as first-line treatment in patients diagnosed with polycythemia vera. Additionally, it emphasizes the impact on hematologic parameters and symptom resolution in both first-line and second-line treatment settings. The second main objective of this study was to illustrate the adverse effects with the most impact on the individuals.

The hematological response was considerable, with approximately 50% achieving the normalization of complete blood count within the first three months of treatment.

Group A – where Besremi was used as first-line treatment, showed a rapid and major favorable response regarding the hemoglobin and hematocrit levels after the first month of treatment. It must be noted that the response after 3 months of treatment was maintained, therefore enforcing its efficiency as first-line therapy for polycythemia vera. In contrast, group B – where Besremi was used as second-line treatment after Hydroxyurea, the data showed a delayed response, with hemoglobin and hematocrit levels normalizing in the majority of the group after 3 months of treatment. It is questioned whether prior exposure to Hydroxyurea may influence the initial response to Besremi.

The platelets reduction was significant in both groups, with a more important decrease overall in group A, which also had higher baseline mean values. Recognizing the increased thrombotic risk in patients with polycythemia vera (observed in 1/5 to 1/3 of the patients [9]), the platelets reduction represents an important achievement of Besremi.

Regarding the white blood count (WBC), the baseline values were higher for group B, being once more questioned whether the abnormal levels were due to the previous administration of Hydroxyurea. After 3 months of treatment, both groups had normal WBC values, highlighting the efficiency of Besremi in leukocytosis control.

Quality of life (QoL) plays a critical role in the management of myeloproliferative neoplasms. A periodic MPN-10 test shall improve QoL assessment in patients with myeloproliferative disorders. Our patients underwent periodic testing (every 2/3 months) for a better analysis of symptoms resolution. Our study demonstrates the effectiveness of Besremi in enhancing QoL, with 13 patients achieving complete symptom resolution and 3 experiencing partial improvement. Nonetheless, the persistence of symptoms in certain patients, such as splenomegaly, highlights the importance of personalized symptom management and the need for further refinement of treatment strategies.

In regards to the adverse effects, our findings support the literature. The most common adverse events were fatigue and headaches, but we could not certainly attribute these to the Besremi treatment. 4 subjects showed important changes in their biological and haematological blood work, with grade 3/4 adverse effects. Hepatotoxicity was one of the most notable adverse effects on this study, with a resolution of the transaminase anomalies after decreasing or stopping the treatment, emphasising the direct effect of Besremi on the hepatic activity. Moderate anaemia was another important haematological adverse effect, the subject being switched to a third-line treatment option – Ruxolitinib. Lastly, one patient with prior utilization of Hydroxyurea as a treatment option for polycythemia vera, after being switched to Besremi, did not achieve a favorable haematological response. We decided to reintroduce Hydroxyurea in addition to Besremi, and monitor the patient closely for the first 3 months of treatment. The data mostly correlates with other studies previously performed, with leukopenia and thrombocytopenia being the main exceptions. We did encounter 1 patient in group A with a mild thrombocytopenia (140 000/mm³), while group B had 2 individuals with leukopenia and one with thrombocytopenia. One patient in group B also experienced neutropenia as a side effect to the administration of Besremi [5,9-11].

The results highlight the efficiency of Besremi as first-line therapy option by achieving a rapid and important hematologic control and symptom resolution. Regarding

the patients that have been priorly exposed to other treatments (Hydroxyurea), a delayed response should be anticipated and close monitoring is needed in the initial treatment period.

In CONTINUATION-PV study, it is enforced that a more impressive response after long-term treatment with Besremi, with an improved haematological response after 36 months in approximately 50% of the patients compared to Hydroxyurea treatment. Another study was performed that evaluated the efficacy of Besremi after 5 years of treatment, as an extension to the CONTINUATION-PV study. After 2 more years of treatment, it is noted an increase in the haematological response up to 55.8% [5,8, 10-12].

Additionally, data from PROUD-PV also enforces the non-inferiority of Ropeginterferon alfa-2b to Hydroxyurea, showing that both treatments achieve a complete hematological response [12].

There are multiple limitations to this study, the first one being the small number of patients included. Additionally, incomplete follow-up data for almost a third of the patients limits the assessment long term. It must be mentioned that the 6 month and 1 year follow up was initially included in the study, but the insufficiency of data was deemed as a pertinent reason to exclude from the graphics and results. Future studies with larger cohorts are needed in order to validate these results and explore the long term efficacy and safety of Besremi.

Conclusion

Besremi (Ropeginterferon) represents a new improved therapy option for the treatment of polycythemia vera with a longer half life and a favorable safety profile.

This study emphasized its efficacy regarding achieving complete response when used as a first-line treatment, while also illustrating its effects when used as a second-line treatment.

As observed, we can see that the results are faster when used as first-line, with immediate response after the first

month of treatment regarding the hemoglobin and hematocrit levels and with important decrease in platelets levels thus lowering thrombotic risk.

When being administered as a second line therapy, one can expect a delayed response and must monitor closely at the start of therapy in order to best assess if there is only a delayed response or an intolerance/resistance to the drug.

Regarding the quality of life, the majority of the patients have experienced complete resolution, and 3 patients' partial resolution of symptoms, which further highlights the efficacy of Besremi in the treatment of polycythemia vera.

The adverse events are diverse, most frequently met being fatigability, asthenia, headaches. In regards to high grade events, the most remarkable mentions are hepatotoxicity and haematological modification. A small number of patients experienced leukopenia, thrombocytopenia, neutropenia, but contrary to the literature, were not the most frequent.

The limitations of the study are notable, the small study cohort and the short term observation of the patients being the most important ones. Further studies on larger cohorts and for a longer period of time should be performed in order to confirm the findings of this study and the favorable safety profile in the long term.

Additionally, different studies can be performed on the effects of Hydroxyurea used prior to the administration of Besremi in order to illustrate if there is an association between the delayed response (as observed in Group B) and Hydroxyurea treatment.

Conflicts of interest

"This research did not receive any grant from agencies in the public, commercial, or not-for-profit sectors.

None of the authors has any conflict of interest.

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national laws. Informed consent was obtained from all the patients included in the study."

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