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Comparison of intravenous and subcutaneous administration of ocrelizumab. Time and motion study

Porównanie podania dożylnego i podskórnego okrelizumabu. Badanie efektywności pracy

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Abstract

Introduction and objective: Ocrelizumab is used in multiple sclerosis treatment and is available in intravenous and subcutaneous forms. In Poland, only the intravenous form is currently reimbursed. The subcutaneous form offers a shorter administration time, potentially benefiting both healthcare providers and patients. This study evaluates the impact of the different forms of ocrelizumab administration on medical facility workflow and costs. **Materials and methods:** A survey was conducted in six medical centres involving 329 patients treated with ocrelizumab in 2023, with 46 patients receiving the subcutaneous form of the drug. The study assessed the complete drug administration process, including premedication, preparation, administration, and post-administration observation. The comparison between the two forms of ocrelizumab focused on the costs associated with drug administration, the time patients spent at the medical centre, and the efficiency of the drug administration process. **Results:** The administration costs of the subcutaneous form were significantly lower (96.80 PLN) than the intravenous form (224.32 PLN). The time patients spent at the medical centre was greatly reduced for the subcutaneous form (56 minutes) compared to the intravenous form (242 minutes). Efficiency in drug administration was also higher for the subcutaneous (26.88) than the intravenous form (2.62). **Conclusions:** The study highlights the substantial benefits of the subcutaneous form of ocrelizumab over the intravenous form. These advantages are noticeable from both the healthcare provider's and patient's perspectives, underscoring the potential for improved efficiency and patient experience with the subcutaneous form.

Keywords: multiple sclerosis, ocrelizumab, costs and cost analysis

Streszczenie

Wprowadzenie i cel: Okrelizumab to lek stosowany w leczeniu stwardnienia rozsianego, dostępny w dwóch formach: dożylnej i podskórnej. Obecnie w Polsce refundowana jest tylko forma dożylna. Forma podskórna oferuje krótszy czas podania, co może przynieść korzyści zarówno ośrodkom medycznym, jak i pacjentom. Niniejsze badanie ocenia wpływ formy podania okrelizumabu na organizację pracy ośrodków medycznych i związane z tym koszty. **Materiał i metody:** Przeprowadzono badanie ankietowe, w którym udział wzięło sześć ośrodków medycznych o łącznej liczbie 329 pacjentów leczonych okrelizumabem w 2023 roku, w tym 46 pacjentów otrzymujących formę podskórną. W badaniu uwzględniono cały proces podania leku obejmujący: premedykację, przygotowanie leku, jego podanie oraz obserwację po podaniu. Obie formy okrelizumabu porównano pod kątem kosztów związanych z podaniem, czasu spędzanego przez pacjentów w ośrodku medycznym oraz efektywności procesu podania leku. **Wyniki:** Koszty podania formy podskórnej były znacząco niższe (96,80 PLN) w porównaniu z formą dożylną (224,32 PLN). Czas spędzony przez pacjentów w ośrodku medycznym był znacznie krótszy przy podaniu podskórnym (56 minut) w porównaniu z dożylnym (242 minuty). Wydajność ośrodków medycznych również była wyższa dla formy podskórnej (26,88) niż dla postaci dożylnej (2,62). **Wnioski:** Badanie wykazało

znaczące korzyści formy podskórnej okrelizumabu w porównaniu z formą dożylną. Zalety są zauważalne zarówno z perspektywy ośrodków medycznych, jak i pacjentów. Zastosowanie formy podskórnej przyczyni się do poprawy wydajności ośrodków medycznych i doświadczeń pacjentów związanych z podaniem leku.

Słowa kluczowe: stwardnienie rozsiane, okrelizumab, koszty i analizy kosztowe

INTRODUCTION

Ocrelizumab stands as the first and only anti-CD20 monoclonal antibody (mAb) dedicated for the treatment of relapsing and primary progressive multiple sclerosis (MS), approved by European Medicines Agency in 2018 (European Medicines Agency, 2024). The safety and efficacy of the drug has been demonstrated through three randomised, double-blind clinical trials: OPERA I, OPERA II for relapsing multiple sclerosis (RMS), and ORATORIO for primary progressive multiple sclerosis (PPMS). These studies confirmed ocrelizumab's ability to inhibit clinical and radiological disease activity and progression, enabling patients to maintain physical and cognitive functions while avoiding disability over the long term (Hauser et al., 2017; Montalban et al., 2017). Although ocrelizumab can be administered either intravenously (IV) or subcutaneously (SC), only the IV form is currently reimbursed in Poland. Despite the availability of the more convenient SC form on the market, it is not reimbursed (Ministerstwo Zdrowia, 2024). Ocrelizumab has been available in Poland as part of a drug programme for treating MS since November 2019 [II line in relapsing-remitting multiple sclerosis (RRMS), and the only drug in PPMS], and since July 2023 in I line for RRMS (Agencja Oceny Technologii Medycznych i Taryfikacji, Wydział Taryfikacji, 2024; Ministerstwo Zdrowia, 2024). In 2023, 2,000 patients received ocrelizumab IV (Narodowy Fundusz Zdrowia, 2024b).

Intravenous administration requires a substantial time commitment. The initial dose consists of two infusions given two weeks apart, each lasting approximately 2.5 hours. The subsequent doses are administered as single infusions every six months, each lasting around 3.5 hours (European Medicines Agency, 2024). For patients without serious infusion-related reactions (IRR) from previous infusions, the administration time may be shortened to 2 hours (European Medicines Agency, 2024; Hartung et al., 2024). However, when factoring in the time required for premedication (typically 30–60 minutes before each infusion) and the mandatory one-hour post-administration observation period, patients are often required to spend 4–5 hours in a hospital for each treatment session.

In contrast, the alternative subcutaneous administration involves a quick 10-minute injection in the abdomen, with oral premedication administrated shortly beforehand. A one-hour observation is required only after the initial dose (European Medicines Agency, 2024). This approach significantly reduces the time and effort required from both patients and medical staff, often to just a few minutes.

The shorter administration time of the subcutaneous form offers undeniable advantages. For MS patients, this reduction in time spent at the medical centre not only improves their quality of life (QoL), but also eases the burden on their caregivers. The subcutaneous mode reduces the clinical and social burden on a group already heavily impacted by MS. According to Professor Krzysztof Selmaj, Director of the Centre of Neurology in Łódź and head of the Department of Neurology at the University of Warmia and Mazury in Olsztyn, the subcutaneous form of the drug offers significant benefits by reducing the time patients need to spend at the hospital, enabling them to maintain their occupational activities without disruption (Wójcik and Selmaj, 2023). Additionally, the SC mode simplifies the premedication process, requiring only easy-to-administer oral premedication, compared to the intravenous form, which necessitates both oral antihistamines and IV methylprednisolone administrated 30-60 minutes before infusion (European Medicines Agency, 2024).

The subcutaneous mode results in reduced consumption of drugs and medical materials required for preparing and administering the drug, while also decreasing the time the drug administration station is occupied. This improvement translates into a greater efficiency of the station (daily number of drug administrations/patients treated). From the healthcare provider's perspective, the new subcutaneous form may minimise the involvement of medical personnel in the procedure and lower the costs associated with drug administration. So far, a multinational clinical study has demonstrated the non-inferiority of the SC versus the IV mode of administration in terms of pharmacokinetics, magnetic resonance imaging (MRI) activity, and clinical relapses (Newsome et al., 2024). The safety profiles of both ocrelizumab forms are comparable, except for the occurrence of reactions characteristic for the form of administration, including injection- or infusion-related reactions (Selmaj and Selmaj, 2023).

The aim of this study is to examine the impact of ocrelizumab administration on the operational workflow of medical facilities and the associated costs, depending on the method of administration. Specifically, the study focuses on how the form of administration affects the duration of the patient's stay, the involvement of medical staff, and the consumption of resources.

METHODOLOGY

To compare the administration of ocrelizumab in its intravenous and subcutaneous forms, a survey was conducted across six healthcare providers. In 2023, these medical centres treated

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a total of 329 patients with ocrelizumab, of whom 46 patients received the SC form. The survey covered the entire drug administration process, encompassing the following stages:

1. premedication before drug administration;
2. drug preparation;
3. drug administration;
4. patient's observation after administration.

The healthcare providers were asked to provide information on:

- resources utilised (medical personnel, medical materials, drugs for premedication);
- time patients spent in the medical centre for drug administration;
- available infrastructure (number of drug administration stations).

Based on the responses, a comparative analysis of IV and SC ocrelizumab administration was conducted, focusing on:

- costs associated with drug administration (medical staff engagement, premedication drugs, and medical materials);
- time patients spent in the medical centre during drug administration;
- efficiency of drug administration stations (average number of drug administrations during a typical workday).

The research findings were derived from the data provided by the participating healthcare providers. However, due to incomplete information regarding medical staff salaries, and costs of premedication drugs and medical materials, supplementary data were sourced as follows:

- medical staff salaries: values were estimated using average salaries of medical personnel, as reported by Agencja Oceny Technologii Medycznych i Taryfikacji, Wydział Taryfikacji (Agency for Health Technology Assessment and Tariff System, AHTATS) (Agencja Oceny Technologii Medycznych i Taryfikacji, Wydział Taryfikacji, 2024);
- premedication drug doses: referenced from the Ocrevus Product Information (European Medicines Agency, 2024); the cost of 1 mg of premedication substances was calculated as a weighted average (based on the number of reimbursed milligrams) of the wholesale prices of reimbursed drugs containing the active substance, as listed in the Ministry of Health's announcement on reimbursed drugs (Ministerstwo Zdrowia, 2024);
- number of reimbursed milligrams: based on the number of packages sold between May 2023 and April 2024 (Narodowy Fundusz Zdrowia, 2024a);
- amount of medical materials used during drug administration: estimated from information obtained from two healthcare providers, with the cost of individual materials sourced from an online medical supplies store (Matopat, materiały opatrunkowe i opatrunki specjalistyczne, 2024).

The engagement time of medical staff, the duration of patient stay at the medical centre, and the number of drug administration stations were calculated as the average results from surveys.

RESULTS

Medical staff engagement

The total time of the doctor's involvement in administering the drug intravenously was approximately 29 minutes, while the subcutaneous administration took more than half the time, around 12 minutes. The time savings were even more pronounced for nurses, with IV administration requiring 74 minutes versus just 28 minutes for SC (over 2.5 times faster). The most significant differences (nearly 16 minutes) occurred during the nurse's involvement in premedication and drug administration (Tab. 1).

The average cost of medical staff involvement was determined by calculating the average time spent on drug administration and applying the average hourly wage of medical staff: 170.77 PLN for doctors and 92.48 PLN for nurses (Agencja Oceny Technologii Medycznych i Taryfikacji, Wydział Taryfikacji, 2024).

The total staff engagement costs for administering the drug intravenously amounted to 196.41 PLN. In contrast, the costs of subcutaneous administering were significantly lower, by 118.78 PLN, amounting to 77.64 PLN (Tab. 2).

Stage of drug administration procedure	Medical staff	Average time [min.]		
		Ocrelizumab IV	Ocrelizumab SC	IV vs. SC difference
Premedication	Doctor	8.67	4.00	4.67
	Nurse	21.67	5.75	15.92
Drug preparation	Nurse	13.75	6.38	7.37
Drug administration	Doctor	13.81	4.00	9.81
	Nurse	26.19	10.38	15.81
Patient's observation after administration	Doctor	6.26	4.25	2.01
	Nurse	12.76	5.25	7.51
Total	Doctor	28.74	12.25	16.49
	Nurse	74.37	27.76	46.61

IV – intravenous; **SC** – subcutaneous.

Tab. 1. Average time of medical staff involvement in the ocrelizumab administration procedure

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Stage of drug administration procedure	Medical staff	Average costs		
		Ocrelizumab IV	Ocrelizumab SC	IV vs. SC difference
Premedication	Doctor	24.67 PLN	11.38 PLN	13.29 PLN
	Nurse	33.40 PLN	8.86 PLN	24.54 PLN
Drug preparation	Nurse	21.19 PLN	9.83 PLN	11.36 PLN
Drug administration	Doctor	39.31 PLN	11.38 PLN	27.93 PLN
	Nurse	40.37 PLN	15.99 PLN	24.38 PLN
Patient's observation after administration	Doctor	17.82 PLN	12.10 PLN	5.72 PLN
	Nurse	19.67 PLN	8.09 PLN	11.58 PLN
Total		**196.41 PLN**	**77.64 PLN**	**118.77 PLN**
IV – intravenous; **SC** – subcutaneous.				

Tab. 2. Average costs of medical staff involvement in the ocrelizumab administration procedure

Parameter	Average costs		
	Ocrelizumab IV	Ocrelizumab SC	IV vs. SC difference
Premedication drugs	7.11 PLN	14.23 PLN	–7.12 PLN
Medical materials for premedication	10.40 PLN	0.00 PLN	10.40 PLN
Medical materials for drug administration	10.40 PLN	4.93 PLN	5.47 PLN
Total	**27.91 PLN**	**19.16 PLN**	**8.75 PLN**
IV – intravenous; **SC** – subcutaneous.			

Tab. 3. Average costs of premedication drugs and medical materials for ocrelizumab administration procedure

Premedication drugs and medical materials

The total costs of premedication drugs for ocrelizumab IV were 7.11 PLN, while for ocrelizumab SC, these costs were more than double, amounting to 14.23 PLN. The costs of medical materials were calculated for both forms and for the premedication of ocrelizumab IV, with intravenous premedication requiring additional materials. It was assumed that oral drugs used in premedication do not require any medical materials, resulting in a cost of 0 PLN for ocrelizumab SC premedication.

Overall, the total costs of medical materials for ocrelizumab SC were more than four times lower than for ocrelizumab IV (4.93 PLN vs. 20.80 PLN). This difference arises not only from the materials used during administration but also from the disparity in costs of medical materials required for premedication (10.40 PLN for IV vs. 0 PLN for SC). Consequently, the combined costs of premedication drugs and medical materials for ocrelizumab SC are lower than for ocrelizumab IV (19.16 PLN vs. 27.91 PLN) (Tab. 3).

Patient time spent at the medical centre

The time patients spent undergoing the drug administration procedure was significantly shorter for ocrelizumab SC at every stage. The total duration of a patient's stay for intravenous administration was 242 minutes, whereas the subcutaneous form required only 56 minutes – four times shorter (over 3 hours difference). The greatest time difference was observed during the drug administration stage itself: administering ocrelizumab SC took just 9.3 minutes, while ocrelizumab IV took more than 15 times longer (146.7 minutes) (Tab. 4).

Efficiency of drug administration station

The efficiency of the drug administration station was defined as the average number of drug administrations possible during a unit's workday. The time used for drug administrations in one workday was assumed to be 7 hours, as patients undergo premedication (30–60 minutes before administration), within an 8-hour workday for the unit. The occupation time for each administration was calculated as the combined duration of the patient's stay during drug administration and the time required by the nurse to prepare the drug (Tab. 5).

The efficiency of a single drug administration station for ocrelizumab SC is more than 10 times greater than that for ocrelizumab IV.

The survey results indicated that the average number of stations for administering intravenous drugs (volumetric pumps) in a unit is 3, while the average number of stations for administering subcutaneous drugs (syringe pumps) is 1. An analysis of the overall efficiency of all stations at the unit (3 stations for ocrelizumab IV and 1 station for ocrelizumab SC) revealed that, despite having three times more stations for intravenous administration, it is possible to perform 19 more administrations of the subcutaneous form than the intravenous form in a single workday. The number of drug administrations directly translates to the number of

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Stage of drug administration procedure	Average time [min.]		
	Ocrelizumab IV	Ocrelizumab SC	IV vs. SC difference
Premedication	46.67	29.00	17.67
Drug administration	146.67	9.25	137.42
Patient's observation after dosing	49.00	17.50	31.50
Total	**242.33**	**55.75**	**186.58**
IV – intravenous; **SC** – subcutaneous.			

Tab. 4. Average patient time in the medical centre during ocrelizumab administration procedure

Parameter	Ocrelizumab IV	Ocrelizumab SC	IV vs. SC difference
Average occupation time of 1 station for 1 drug dosing (drug preparation + drug administration)	160.42 min.	15.63 min.	**144.79 min.**
Efficiency of 1 station during 1 workday (7 hours)	2.62	26.88	**–24.26**
IV – intravenous; **SC** – subcutaneous.			

Tab. 5. Average efficiency of one drug administration station during ocrelizumab administration procedure

Number of drug administrations for all stations during:	Ocrelizumab IV (3 stations)	Ocrelizumab SC (1 station)	IV vs. SC difference
1 workday (7 hours)	7.85	26.88	**–19.03**
1 workweek (5 workdays)	39.27	134.40	**–95.13**
IV – intravenous; **SC** – subcutaneous.			

Tab. 6. Average efficiency of all drug administration stations in standard unit (3 stations for ocrelizumab IV administration and 1 station for ocrelizumab SC administration)

patients who can be treated. Thus, in one workday at a standard unit, approximately 27 patients can receive the subcutaneous drug at one station, whereas only about 8 patients can be treated with the intravenous drug at 3 stations.

Over a one-week period (5 workdays), the difference becomes even more pronounced, amounting to 95 additional drug administrations. The weekly total for ocrelizumab IV at 3 stations is approximately 39 administrations, while for ocrelizumab SC at one station, the total is about 134 administrations (Tab. 6).

DISCUSSION

The use of ocrelizumab in subcutaneous form offers numerous advantages over the intravenous form, benefiting both the patient and the healthcare provider. It is important to emphasize the equal level of efficacy and safety for both drug forms.

The survey results highlighted significant savings for the healthcare provider when administering ocrelizumab subcutaneously compared to intravenously. The total cost of the administration procedure (including personnel engagement and the costs of premedication drugs and medical materials) was more than twice as low for the SC form compared to the IV form (96.80 PLN vs. 224.32 PLN). Similar costs savings have been observed with other MS drug (e.g. natalizumab), where a Spanish cost analysis reported a cost reduction of 66.2–69.8% when switching from IV to SC administration (Alonso Torres et al., 2023).

Significant time savings for medical staff were also evident, with doctors saving 16.5 minutes and nurses 46.6 minutes per administration when using the SC drug form. The time saved by medical personnel would allow for the treatment of a larger number of patients and contribute to a significant increase in the efficiency of the unit. This saved time could also be used for patient education. Research results showed more than ten times higher efficiency of one administration station for the subcutaneous drugs compared to the intravenous drugs (26.88 SC administrations/workday vs. 2.62 IV administrations/workday).

In this context, the Irish experience is worth noting, as it suggests that the introduction of subcutaneous ocrelizumab could expedite access to this medication for MS patients, who currently face long wait times for intravenous treatment. This change could help reduce delays and improve outcomes for people living with MS (Multiple Sclerosis Society of Ireland, 2024).

From the patient's perspective, the form of administration is crucial. Subcutaneous administration significantly reduces the time spent at the medical centre compared to intravenous administration (56 minutes vs. 242 minutes). Often, considering travel time, a visit associated with drug administration requires devoting an entire day, leading to absences from work for both patients and their caregivers. The shorter duration of SC administration could allow patients and caregivers to maintain their occupational activities. Conclusions drawn by representatives of Johns Hopkins Medicine highlighted similar benefits for the subcutaneous form of ocrelizumab. They noted that access to intravenous administration can be challenging for some patients, particularly those who do not live near an infusion centre or have poor venous access. Additionally, some MS centres have limited IV capacity or lack IV infrastructure altogether. Consequently, the 10-minute subcutaneous

ocrelizumab injection could potentially broaden access to more patients who could benefit from this highly effective therapy (Meglio, 2024).

CONCLUSION

The survey results clearly demonstrate the significant benefits of the subcutaneous form of ocrelizumab compared to the intravenous form. From the healthcare provider's perspective, SC administration reduces costs by more than half (96.80 PLN vs. 224.32 PLN) and achieves over tenfold higher efficiency in drug administration stations (26.88 SC administrations/workday vs. 2.62 IV administrations/workday). From the patient's perspective, subcutaneous administration shortens the time spent at the medical centre by approximately 3 hours (56 minutes vs. 242 minutes). In conclusion, the subcutaneous form of ocrelizumab presents a compelling alternative to the intravenous form, offering substantial benefits in terms of both time efficiency and cost reduction.

Conflict of interest

E. Krzystanek has received remuneration for consultations and participation in advisory board meetings from Biogen, Merck Serono, Bayer, Roche, Novartis, and the Polish Multiple Sclerosis Society; served as a principal investigator (PI) for clinical trials for Roche, TG Therapeutics, Merck, Biogen, Lundbeck, and Janssen; and delivered lectures for Biogen, Bayer, Novartis, UCB, Roche, Merck Serono, Teva, Lundbeck, Pfizer, Sandoz, Sanofi Genzyme, Grindex, and Alfasigma.

B. Rękawek is an employee of a consulting company conducting pharmacoeconomic projects for pharmaceutical companies, including Roche.

K. Selmaj has received remuneration for participation in scientific committees of clinical trials, consultations, and advisory board meetings from Novartis, Roche, Merck, TG Therapeutics, Bristol Myers Squibb, Biogen, Neuraxpharm, Astra, Sandoz, and for invited lectures from Biogen, Roche, Novartis, Merck, Astra, Sandoz, and Bristol Myers Squibb.

M. Seweryn is the owner of a consulting company conducting pharmacoeconomic projects for pharmaceutical companies, including Roche.

The remaining authors have not declared any conflict of interest.

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Author contribution

Original concept of study; analysis and interpretation of data: BR, MS. Collection, recording and/or compilation of data; final approval of manuscript: EK, KS, BR, IS, AK, PB. Writing of manuscript: EK, BR, MS. Critical review of manuscript: EK, KS, IS, AK, PB, MS.

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