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Advantages of Rapid Rituximab Administration in Oncology. Study and Analysis in Real Clinical Settings in Poland - Hospital Based HTA Project

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Abstract

Objective: Rituximab, a chimeric monoclonal antibody targeting CD20 on B lymphocytes, has revolutionized hematologic malignancy treatment since its FDA and EMA approvals in 1997 and 1998. For a long time, rituximab treatment has been the standard for follicular lymphoma (FL), diffuse large B-cell lymphoma, and chronic lymphocytic leukemia (CLL), significantly improving survival rates and quality of life. Rapid intravenous infusions, approved by the FDA in 2012 and EMA in 2023, reduce infusion times to 90 minutes, offering similar safety profiles to standard infusions with significant cost savings and reduced strain on healthcare resources. This analysis evaluates the benefits of rapid rituximab administration in Poland using Hospital-Based Health Technology Assessment (HB-HTA) methodology. Methods: Conducted from December 2023 to January 2024, the study involved 155 observations of standard infusions across 14 centers in Poland. Medical personnel completed forms detailing rituximab administration stages and patient information. Data were used to develop an economic model assessing the benefits of 90-minute infusions, replacing the observed standard delivery, considering setup time, medical personnel involvement, and hospital savings. Supplementary qualitative data were collected through 9 in-depth telephone interviews with medical personnel and patients. Results: The study included 155 patients with an average age of 61 years and an average infusion duration of 3 hours and 46 minutes. It is estimated that replacement of standard delivery with rapid infusions could save 21.47 PLN labor costs per infusion for CLL patients and 25.04 PLN for NHL patients, as well as would reduce bed occupancy and free up medical staff time. This is expected to allow the increased number of infusions to be performed monthly and allow for resource reallocation. Nurses expressed positive opinions on the benefits of rapid infusions, highlighting, among other things, reduced patient wait times and improved operational efficiency in ward operations Conclusions: Rapid rituximab infusions potentially would enhance patient convenience, healthcare resource efficacy, and reduce costs in the Polish healthcare sector setting. They also could improve patient quality of life by minimizing time in medical facilities. The adoption of rapid administration protocols can transform oncology practice, making it more efficient and patient-oriented. To fully realize these benefits, modifications to the NHF catalogue and public procurement criteria are recommended, along with developing outpatient care to reduce administrative burdens and relieve hospital resources.

Abbreviations: CHP - cyclophosphamide, doxorubicin, and prednisone regimen; CLL - chronic lymphocytic leukemia; EMA - European Medicines Agency; FDA - US Food and Drug Administration; FL - follicular lymphoma; FTE - full-time equivalent; HB-HTA - Hospital-Based Health Technology Assessment; IRRs - Infusion-related reactions; NHF - National Health Fund; NHL - non-Hodgkin lymphoma.

1. Introduction

1.1 Background information on rituximab use in oncology

Rituximab, a chimeric monoclonal antibody targeting the CD20 antigen on B lymphocytes, has significantly transformed the therapeutic landscape of hematologic malignancies since its approval in 1997 by the US Food and Drug Administration (FDA) and in 1998 by the European Medicines Agency (EMA).[1,2] Initially developed for the treatment of non-Hodgkin lymphoma (NHL), rituximab has expanded its indications to other B-cell malignancies, as well as autoimmune diseases such as rheumatoid arthritis.[1,2,3,4] Intravenous rituximab was the first monoclonal antibody to be approved for the hematological cancers treatment and has paved the way for the development of other monoclonal antibodies and targeted therapies.[1,5]

In nearly 30 years since its market introduction, intravenous rituximab has long been the standard of care, and it remains an important component of treatment for follicular lymphoma,[6,7,8] diffuse large B-cell lymphoma[9,7,10], and chronic lymphocytic leukemia.[11,12,13] It is also a crucial element of new treatment regimens in hemato-oncology, such as the rituximab + venetoclax regimen in CLL[14] or polatuzumab + rituximab + CHP (cyclophosphamide, doxorubicin, and prednisone) regimen in diffuse large B-cell lymphoma.[15] Additionally, it is included in protocols that are still in the research stage but have shown promising results, such as the epcoritamab + rituximab + lenalidomide regimen in FL[16] and the epcoritamab + polatuzumab + rituximab + CHP regimen in diffuse large B-cell lymphoma.[17] Patients treated with rituximab-containing regimens have experienced significant improvements in survival rates and quality of life. The ability to

target B cells specifically has allowed for more effective and less toxic treatment options compared to traditional chemotherapy alone.[1,2]

Biosimilar products have also been introduced to the market, increasing drug accessibility while maintaining safety and efficacy standards, and simultaneously reducing therapy costs.[18] Since its introduction, research has been exploring new formulations and administration methods for rituximab to further enhance its efficacy and convenience, including the subcutaneous form of rituximab.

Traditional rituximab administration protocols require prolonged infusion times, often extending several hours, which can be burdensome for both patients and healthcare facilities. Rapid rituximab administration protocols, which reduce infusion times to as little as 90 minutes, have been developed to address these challenges. One of such advancements has been the introduction of rapid intravenous infusions of rituximab. In 2012, the FDA approved a 90-minute infusion of rituximab for previously untreated patients with follicular NHL or diffuse large B-cell lymphoma.[3] In Europe, 90-minute infusions were approved by the EMA more recently in 2023 for the treatment of NHL or CLL.[19]

1.2 Clinical efficacy and safety of rapid infusion of rituximab in oncology

In Europe, intravenous rituximab can be administered to patients with NHL and CLL using two infusion protocols: so-called standard and rapid infusion. The recommended initial infusion rate for both protocols is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, up to a maximum of 400 mg/h. Subsequent doses of rituximab during the standard infusion protocol can be administered at an initial rate of 100 mg/h, increasing by 100 mg/h increments at 30-minute intervals, up to a maximum of 400 mg/h. If patients do not experience a Grade 3 or 4 infusion-related adverse event during Cycle 1, instead a rapid infusion protocol can be used, in which 90-minute infusion can be administered in Cycle 2 with a glucocorticoid-containing chemotherapy regimen. The infusion should be initiated at a rate of 20% of the total dose given in the first 30 minutes, with the remaining 80% administered over the next 60 minutes. If the 90-minute infusion is tolerated in Cycle 2, the same rate can be used for the remainder of the treatment regimen (through Cycles 6 or 8). Patients with clinically significant cardiovascular disease, including arrhythmias, or those with previous serious infusion reactions to any prior biologic therapy or to rituximab, should not receive the rapid infusion.[20]

Clinical studies have demonstrated that rapid rituximab infusions are generally well tolerated, with similar safety profile to standard infusion protocol. Studies comparing rapid and standard administration protocols have demonstrated that rapid administration is equally safe and effective[21,22,23], with no significant differences in the incidence of infusion-related reactions (IRRs) or other adverse events.[24] In comparative studies, the incidence of IRRs was similar between rapid and standard rituximab infusions. In a prospective study involving 550 patients with NHL, IRRs following the first infusion occurred in 4.16% of patients receiving rapid infusion and 6.04% of patients receiving slow infusion.[25] Another study compared 40 NHL patients treated prospectively with rapid infusion rituximab (non-initial infusion) to 30 patients in a retrospective group treated with conventional infusion, finding no significant difference in IRR rates between the two groups.[26] The prospective MAXIMA study in patients with FL receiving maintenance rituximab showed comparable IRR rates between those who received all standard rate infusions (n=370; 5.4%) and those who received all rapid infusions (n=82; 4.9%).[23] Additionally, in a prospective study of patients receiving non-initial rituximab infusions, IRRs were observed in 3% of 37 patients treated with rapid infusion and 4% of 27 patients treated with non-rapid infusion.[27]

1.3 Potential Benefits of Rapid Rituximab Administration in Clinical Practice

Long infusion times and frequent rate adjustments result in increased workloads for nursing and administrative staff, and inconvenience for patients.[28] In healthcare settings with limited resources, such as chair space and nursing workforce, this can lead to longer wait times for treatment administration.[29] Lengthy infusion schedules also incur high treatment costs for payers.[29] The rationale for exploring rapid administration includes enhancing patient convenience, optimizing resource utilization, and increasing the efficiency of infusion centers. The implementation of rapid rituximab infusions significantly reduced administration times and nursing workload.[30,31,32,33,34,35] Medical personnel have expressed a preference for rapid administration due to the reduced strain on healthcare resources and the potential for increased patient throughput.[36,32,37] Furthermore, studies conducted in different countries have demonstrated significant cost savings associated with the adoption of the 90-minute rituximab infusion. Economic evaluations have highlighted the reduction in direct medical costs and indirect costs, such as patients' foregone income due to time spent on infusions.[38,31,39,40]

1.4 Purpose of the Analysis

The primary purpose of this analysis was to evaluate the potential benefits of rapid rituximab administration from a hospital perspective in Poland. By employing Hospi-

tal-Based Health Technology Assessment (HB-HTA) methodologies, we aimed to assess the possible impact of rapid administration on resource utilization and overall hospital efficiency. This analysis provided a comprehensive understanding of the potential advantages of adopting rapid rituximab protocols, including optimized use of healthcare resources and potential cost savings from the perspective of the healthcare provider. The findings offered valuable insights for healthcare decision-makers, guiding the implementation of rapid administration protocol and informing policy decisions at the institutional level.

1.5 PICO framework

The PICO (Population, Intervention, Comparison, Outcome) framework was utilized to structure the analysis, focusing on the following elements:
Population: Patients with NHL or CLL receiving intravenous rituximab in Poland. This population includes both newly diagnosed patients and those undergoing maintenance therapy.
Intervention: Rapid rituximab administration, defined as infusion times reduced to 90 minutes, compared to standard administration protocol.
Comparison: Standard rituximab administration, involving traditional infusion times of several hours.
Outcome: resource utilization (infusion center capacity and healthcare costs).
Population and intervention considered were in line with conducted quantitative and qualitative studies, alongside the measured outcomes. The comparator arm was modelled based on assumptions explained in details later on, which based on the converted results from the research studies as well as literature data.

2. Methods

2.1 Methodology of the Quantitative Study

The quantitative study on the treatment of patients with CLL and NHL using rituximab was conducted by IQVIA from December 2023 to January 2024. The aim of the study was to obtain information on the actual data regarding the duration of standard rituximab infusions and the resources used to administer these infusions in centers in Poland (parameters described in Table 1). The study was conducted in 14 centers across Poland and included 155 observations corresponding to administrations of rituximab under the standard infusion regimen (68 observations of patients with CLL and 87 observations of patients with NHL). Medical personnel were recruited at centers where CLL and/or NHL therapy is conducted within drug programs dedicated to CLL or NHL patients, and rituximab is administered. Each respondent was required to complete a minimum of 10 observation forms, which included the times of various stages of rituximab administration and basic patient information, as well as a calendar for 3 consecutive weeks detailing the number of CLL or NHL patients for projection purpose. The observation forms were continuously filled out based on patient visits during the study period.

2.2 Data Analysis Model and Source Data

The data collected through quantitative study were used to develop an economic model aimed at approximating the benefits of switching from standard rituximab infusion to a 90-minute rapid infusion under real-world conditions of the Polish healthcare system. The model was prepared in accordance with the established PICO framework. Due to the shorter infusion duration, particular attention was paid during modeling to the time required for infusion setup, the involvement time of medical personnel, and the resulting savings for the hospital ward from reducing this time.

The primary data source for the model parameters was the previously mentioned quantitative market study conducted by IQVIA. Additional data sources used in the analysis included literature and publicly available databases (e.g., Central Statistical Office), covering aspects such as the average salary of physicians and clinical aspects like the percentage of patients with contraindications to rapid rituximab infusions (parameters are presented in Table 1).

2.3 Supplementary Data from Qualitative Interviews (Case Studies)

The qualitative data were collected through semi-structured interviews with nurses and patients. This study was conducted by IQVIA in January 2024. The research technique employed was in-depth individual telephone interviews (IDIs), with each interview lasting approximately one hour for both nurses and patients. The research sample consisted of 9 IDIs, including 6 IDIs with patients and 3 IDIs with nurses. This study was designed as a case study to provide detailed insights into the perceptions of rituximab infusion methods.

The recruitment criteria for nurses included those working in various medical facilities, caring for hematology patients, and administering rituximab. Specifically, the study focused on nurses who exclusively worked with the standard infusion protocol of rituximab in centers where rapid infusions were not yet used. For patients, the recruitment criteria included individuals with NHL or CLL who received rituximab in multi-hour intravenous infusions, adhering to the standard infusion duration. 3 IDIs were conducted with NHL patients and 3 with CLL patients.

3. Results - Economic and Resource Utilization

3.1 Characteristics of the study population

In the quantitative study, the average age of patients in the sample was 61 years, with NHL patients averaging 63 years [SD: 13.66, range: 30-85] and CLL patients averaging 60 years [SD: 16.80, range: 23-89]. The average weight of the patients was 76.23 kg, with NHL patients averaging 76.91 kg [SD: 18.53, range: 48-135] and CLL patients averaging 75.37 kg [SD: 16.95, range: 44-115]. The percentage of vascular access ports placed was 21%, with 22% for NHL patients and 19% for CLL patients. The average duration of the infusion during the standard protocol was approximately 3 hours and 46 minutes, with NHL patients averaging 243 minutes [SD: 144.0, range 70-700] and CLL patients averaging 204 minutes [SD: 129.6, range 25-660]. This duration was defined as the time from the start of the infusion to its completion.

During each administration of rituximab to a patient with CLL or NHL, a nurse was present. On average, a nurse spent 109 minutes [SD:55, range: 25-245] with the patient, including 42 minutes [SD: 31, range: 10-120] during the rituximab infusion. Physicians participated in half (49% for NHL, 51% for CLL) of the rituximab administrations, with the average time physicians spent being 45 minutes [SD: 36, range: 5-210], including 16 minutes [SD: 17, range: 0-100] during the rituximab infusion. It was also found that other healthcare professionals were minimally involved.

The average number of rituximab vials used was 1.5 vials of 100 mg/10 ml and 1.2 vials of 500 mg/50 ml for NHL patients. For CLL patients, the average number of rituximab vials used was 1.7 vials of 100 mg/10 ml and 1.2 vials of 500 mg/50 ml. Contraindications for the use of rapid infusion in NHL or CLL patients receiving rituximab were rare, occurring in 2% of NHL patients and 7% of CLL patients.

3.2 Cost-Effectiveness of Rapid Rituximab Administration

To estimate resource consumption during the compared hospital interventions, namely the standard rituximab infusion, whose administration time depends on the patient's body weight (comparator, current intervention), and the 90-minute rapid rituximab infusion, in accordance with the Product Characteristics of Riximyo[20] (evaluated intervention), an economic model was prepared, assuming the following input parameters:

- cost data: monthly gross salaries of medical staff (physicians and nurses),
- infusion implementation data: percentages of infusions performed in standard and rapid forms in the current scenario (no availability of rapid rituximab infusions) and the new scenario (availability of rapid rituximab infusions),
- infusion process data: total duration, time involvement of staff (physicians and nurses) at various stages,
- ward data (for demonstration purposes only, a hypothetical ward was analyzed): number of available infusion sites, monthly number of infusions performed, number of nurses and physicians in the ward (parameters described in the Table 1.II.c.).

The values of the parameters adopted in the model, along with their sources of estimation, are presented in the table (Table 1).

Based on the above parameters, the model estimated the average resource consumption (hospital medical staff working time) and the corresponding direct labor costs per single rituximab infusion performed in either the standard or rapid mode. Additionally, benefits at the level of a typical medium-sized hospital were calculated, resulting from replacing a portion of standard infusions with rapid infusions for eligible patients. For the analysis, it was assumed that 90% of infusions in the new scenario would be performed in the rapid mode, considering that for some patients, despite the theoretical possibility of using rapid infusion, it would not be utilized due to factors such as patient preferences. The outcome of this part of the modeling included resource utilization savings, financial benefits, and the impact on the center's throughput.

3.3 Workflow Efficiency and Time Savings

In the CLL patient population, based on the time required by medical staff for an average standard rituximab infusion, each switch to a rapid infusion reduces bed occupancy time by 114 minutes and frees up 28 minutes of nurses and physicians working time. In the existing scenario, assuming only standard rituximab infusions, with the theoretical full occupancy of four infusion sites (assuming ideal rotation), the ward can perform 197 rituximab infusions per month for CLL patients. By switching to rapid infusions in 90% of eligible cases, the ward will be able to perform additional 155 infusions per month (a total of 352 infusions). Switching to rapid rituximab infusions will also free up 2.1% of physicians' total working time and 5.5% of nurses' total working time in the ward. This will allow for the reallocation of 0.1 nurse FTE

Table 1. Parameters used for modeling.		
Parameter	**Value**	**Source of estimation**
I. Cost parameters		
Monthly gross salary of a nurse in Poland	6 865 PLN	Results of a qualitative survey conducted by IQVIA (n=49)
Monthly gross salary of a physician in Poland	12 657 PLN	The median earnings - GUS report on wage structure by occupation for October 2022 (median salary of physicians regardless of place of work) (41)
II. Parameters for the course of infusion and resource consumption		
a) Standard infusion (comparator)		
Duration of infusion	CLL: 204 minutes [SD: 130, range: 25-660] NHL: 243 minutes [SD: 144, range: 70-700]	Results of a qualitative survey conducted by IQVIA (CLL, n=68, NHL, n=87)
Total intervention time*	CLL: 279 minutes [SD: 130, range: 55-685] NHL: 303 minutes [SD: 145, range: 100-760]	Results of a qualitative survey conducted by IQVIA(CLL, n=68, NHL, n=87)
Percentage of infusions requiring physician involvement	CLL: 52.9% NHL: 50.6%	Results of a qualitative survey conducted by IQVIA (CLL, n=68, NHL, n=87)
Total time of nurse involvement in the drug administration procedure**	CLL: 116 minutes [SD: 56, range: 30-245] NHL:103 minutes [SD: 53, range: 25-240]	Results of a qualitative survey conducted by IQVIA (CLL, n=68, NHL, n=87)
including time spent with the patient during the infusion	CLL: 41.5 minutes [SD: 30.6, range: 10-120] NHL: 43.1 minutes [SD: 31.5, range: 10-120]	Results of a qualitative survey conducted by IQVIA (CLL, n=68, NHL, n=87)
Total time of physician involvement in the drug administration procedure**	CLL: 50 minutes [SD: 37, range: 5-210] NHL:40 minutes [SD: 35, range: 5-140]	Results of a qualitative survey conducted by IQVIA (CLL, n=35, NHL, n=43)
including time spent with the patient during the infusion	CLL: 15.1 minutes [SD: 18.7, range: 0-100] NHL:16.2 minutes [SD: 16.5, range: 0-60]	Results of a qualitative survey conducted by IQVIA (CLL, n=35, NHL, n=43)
b) Rapid infusion (evaluated intervention)		
Duration of infusion	CLL: 90 minutes NHL: 90 minutes	Summary of product characteristics of Riximyo (20)
Total intervention time*	CLL: 165 minutes NHL: 150 minutes	Own assumption - time of activity supporting administration equal to corresponding times for standard infusion
Percentage of infusions requiring physician involvement	CLL: 52.9% NHL: 50.6%	Own assumption - as for standard infusions
Total time of nurse involvement in the drug administration procedure**	CLL: 93 minutes NHL: 76 minutes	Own assumption - time of activity supporting administration equal to corresponding times for standard infusion
including time spent with the patient during the infusion	CLL: 18.3 minutes NHL: 16.0 minutes	Own assumption - in proportion to the difference in infusion duration
Total time of physician involvement in the drug administration procedure**	CLL: 41 minutes NHL: 30 minutes	Own assumption - time of activity supporting administration equal to corresponding times for standard infusion
including time spent with the patient during the infusion	CLL: 6.6 minutes NHL: 6.0 minutes	Own assumption - in proportion to the difference in infusion duration
c) Parameters related to the analysis scenario		
Monthly number of rituximab infusions provided by the hospital	60	Own assumption - example parameters to illustrate savings at the ward level
Number of infusion beds/places available in the ward	4	Own assumption - example parameters to illustrate savings at the ward level
Number of nurses available to provide services related to the administration of rituximab	2	Own assumption - example parameters to illustrate savings at the ward level
Number of physicians available to provide services related to the administration of rituximab	1	Own assumption - example parameters to illustrate savings at the ward level
Percentage of patients with contraindications to fast-track infusions	12.5%	RATE study (21) (42)
Percentage of infusions performed by the department on an expedited basis - current scenario***	0%	Own assumption
Percentage of infusions performed by the ward on an expedited basis - new scenario***	90%	Own assumption
Number of working days during the year	251 days	Labor Calendar 2024

** Including the time for preparation, completion, and patient observation post-infusion. ** The total time consists of patient preparation time, time spent with the patient during the infusion, post-infusion care time, and time spent observing the patient after administration. *** Among patients without contraindications for rapid infusion.*

to other tasks performed by the ward, under the assumptions of an exemplary use of the wards' capacity.

At the same time, in the NHL patient population, each switch to a rapid infusion reduces bed occupancy time by 153 minutes and frees up 32 minutes of medical staff (nurses and physicians) working time. In the existing scenario, assuming only standard rituximab infusions and full occupancy of four infusion sites with ideal rotation, the ward can perform 165 infusions per month for NHL patients. Switching to rapid infusions in 90% of eligible cases increases capacity to 328 infusions per month, freeing up 2.4% of physicians' and 6.4% of nurses' working time. This allows for the reallocation of 0.1 nurse FTE to other tasks, under the assumptions of an exemplary use of the wards' capacity.

3.4. Impact on Outpatient Unit Management and Healthcare Resource Utilization

In the CLL patient population the hospital's cost related to salaries was estimated at 112.55 PLN. For the rapid infusion, due to the saved staff time during patient observation during the drug infusion, the salary cost for an average infusion in this mode was estimated at 91.09 PLN. This means that the intervention of replacing standard-duration rituximab infusions with rapid infusions using rituximab in CLL patients allows for a saving of 21.47 PLN per rituximab infusion, solely from medical staff salaries and work time optimization, while maintaining equivalent efficacy and safety profiles.

In the NHL patient population, the hospital's cost related to salaries was estimated at 96.17 PLN. For the rapid infusion the salary cost for an average infusion in this mode was estimated at 71.13 PLN. Replacing standard-duration rituximab infusions with rapid infusions in NHL patients saves 25.04 PLN per infusion, solely from medical staff salaries and work time optimization, while maintaining equivalent efficacy and safety.

Calculating the above at the ward level, with an assumed 60 infusions performed monthly, the estimated direct savings are 1,014 PLN (solely from staff labor costs) per month in the treatment of CLL patients and 1,183 PLN per month in the treatment of NHL patients.

4. Results - quality opinions

4.1 Opinions About Preferences of Medical Personnel and Patients

Nurses participating in the study reported far more benefits from administering the rapid infusion form of rituximab compared to the standard infusion protocol. They noted that shorter patient visits led to reduced waiting time, discomfort, irritation, anxiety, stress, and fatigue. This was particularly beneficial for patients traveling long distances and those accompanied by others. The operational efficiency was improved through streamlined patient admission, reduced nurse workload, and shorter time spend hospitalized or during ambulatory visit. Enhanced safety was achieved by performing infusions with full medical staff presence, increasing patient safety. Resource optimization was noted with greater availability of beds and reduced need for patient admissions, minimizing infection risks. Additionally, the ability to admit more patients enhanced the facility's efficiency. Nurses also noted, that from their perspective, there is a growing number of patients treated with rituximab annually, indicating a demand for more treatment spaces.

The idea of administering rituximab in a rapid 90-minute infusion has polarized patient reactions. For some, it represents a significant time-saving benefit for both the patient and their companions, who can pick up the patient from the hospital sooner or wait shorter. The shorter infusion time leads to a faster return home, reduced waiting times for patients due to quicker patient turnover and has a significant impact during single-day hospitalizations where every hour counts. In contrast, during overnight stays, which may result from the administration of other medications, the infusion time is less critical as it does not expedite discharge. Furthermore, some patients see no justification for switching from the standard to the rapid infusion because it makes no difference for those who need to stay in the ward longer, as a faster rituximab infusion alone does not expedite their return home. Older patients find it difficult to change their habits and are reluctant to alter a therapy that has been effective. Some view the hospital stay as a break from daily activities and prefer to stay longer. For less active individuals or those living alone, the discharge time is not crucial, and they often prefer a longer stay to break their daily routine.

The idea of rapid infusion raised some safety concerns and uncertainty about the body's reaction to the change for some patients. The main concerns of patients receiving the traditional rituximab infusion include potential side effects, effectiveness, and tolerance of the infusion, and questioning if the fast medication is as effective as the standard one. Patients accustomed to slow infusions feel safe and know their

body's reactions, leading to concerns about the safety of the faster infusion. Additionally, patients wonder if their vein condition is suitable for a rapid infusion protocol.

It should be noted that the collected opinions are not statistically significant and are considered as case studies.

4.2 Overall Patient Care and Treatment

Patients participating in the qualitative interviews indicated that the duration of hospital stays varies depending on the facility and the length of the administered infusion, which is often determined by the quantity of medications given. Some patients spend one day at the facility, typically 6-8 hours, while others stay for 2-4 days. This duration is primarily influenced by the organization of visits and the patient flow within the respective facility.

Additionally, the length of hospital stay includes other elements such as registration, medical examinations, administration of the infusion, post-infusion observation, and discharge. These factors are administrative in nature and result from the organization of work within the hospital. Furthermore, the administration of rituximab can occur under various chemotherapy funding schemes, such as outpatient consultation, single-day hospitalization, or full hospitalization.

5. Discussion and Future Directions

The goal of Hospital-Based Health Technology Assessment (HB-HTA) is to support hospital management in making informed decisions about the adoption and use of medical technologies. By evaluating the clinical effectiveness, safety, and cost-effectiveness of new technologies within the specific context of a hospital, HB-HTA helps ensure that resources are used efficiently, and that patient care is optimized. This approach allows hospitals to tailor their technology assessments to their unique needs and circumstances, ultimately improving the quality of care and operational efficiency.

The analysis results demonstrated that the introduction of rapid rituximab infusions (90-minute) for CLL and NHL patients in Poland brings operational and economic benefits to hospitals. Rapid infusions reduce bed occupancy time and medical staff working time. For CLL patients, bed occupancy time decreases by 114 minutes, and staff working time by 28 minutes per infusion. For NHL patients, these values are 153 minutes and 32 minutes, respectively. This change frees up 2.1% of physician' total working time and 5.5% of nurses' total working time for CLL, and 2.4% of physician' and 6.4% of nurses' time for NHL [under the assumptions of an exemplary use of the wards' capacity]. Additionally, the savings in staff working time enable the reallocation of 0.1 nurse full-time equivalent (FTE) to other tasks performed by the ward, potentially improving patient care quality and operational efficiency. Additionally, efficiency is significantly increased, as the number of infusions performed can rise substantially. For CLL patients, the capacity for possible number of infusions increases from 197 to 352 per month, and for NHL patients, from 165 to 328 per month. Financial savings are also notable, with each switch to a rapid infusion generating a saving of 21.47 PLN for CLL patients and 25.04 PLN for NHL patients. This translates to monthly savings of 1,014 PLN and 1,183 PLN, respectively, from direct staff labor costs with an example hospital ward conducting 60 infusions monthly.

It must be underlined, that estimated savings take into consideration only direct labor costs, excluding all other cost categories, that can differentiate between the rapid and standard infusions, such as board and accommodation costs for longer stays in the hospital. Also, in the analysis the alternative costs related to unlocked medical staff time were not considered, which can attribute to additional founds obtained by the hospital due to possibility of engaging in provision of additional healthcare services. Based on the study results and applying HB-HTA assumptions, the introduction of rapid rituximab infusions demonstrates significant potential for enhancing hospital efficiency and patient care. Additionally, these conclusions also seem valid considering the safety profile and the non-differentiating efficacy of administration.

The financial savings observed are substantial, particularly when considering the cumulative effect over time. By reducing the cost per infusion and increasing the number of infusions that can be performed, hospitals can allocate resources more effectively. This is especially important in healthcare settings where budget constraints are a constant challenge. The increase in the number of infusions performed per month highlights the potential for rapid infusions to enhance patient throughput. This is particularly beneficial in high-demand wards where bed occupancy rates are critical. By freeing up bed space more quickly, hospitals can accommodate more patients, potentially reducing wait times and improving overall patient satisfaction. The optimization of staff time is another significant advantage. By reducing the time required for each infusion, medical staff can focus on other critical tasks, thereby improving the overall efficiency of the ward. The reallocation of nurse full-time equivalents (FTEs) to other tasks can lead to better patient care and more efficient use of hospital resources.

Placing the results in the broader context of hemato-oncology care, it is important to note limitations due to the

organization of patient admissions, queuing in the hospital's administrative pathway, waiting times for medication administration, and the different treatment regimens, including other drugs used alongside rituximab. These factors may hinder the full benefits of reduced staff time for rituximab administration. For instance, in the increasingly used R2 (lenalidomide and rituximab) regimen for FL, rituximab is administered intravenously while lenalidomide is oral. In such regimens, examining the patient pathway in the hospital is crucial, as these regimens could yield savings, especially if shifted to ambulatory care. Further studies should focus on the entire patient pathway and the financial aspects, including the conditions for service provision set by the National Health Fund (NHF).

Additionally, research should investigate long-term outcomes associated with rapid rituximab infusions. While the immediate benefits are clear, it is important to assess the long-term impact on patient health outcomes, hospital readmission rates, and overall healthcare costs.

6. Conclusions

The introduction of rapid rituximab infusions was driven by the need to enhance patient convenience, improve healthcare efficiency, and reduce treatment costs. Traditional rituximab infusions, which can take several hours, pose significant logistical challenges for both patients and healthcare providers. Long infusion times can lead to extended hospital stays, increased chair time in infusion centers, and higher overall healthcare costs. By reducing the infusion duration, rapid rituximab protocols aim to alleviate these burdens.

Moreover, rapid infusions can improve patient quality of life by minimizing the time spent in medical facilities, allowing patients to resume their daily activities more quickly. This approach also optimizes resource utilization in healthcare settings, enabling more patients to receive treatment within the same timeframe. The adoption of rapid administration protocols can significantly improve clinical practice and patient care in oncology. By reducing infusion times and optimizing resource use, hospitals can enhance the overall patient experience and achieve cost savings.

Rapid rituximab administration has the potential to transform oncology practice, making it more efficient and patient-oriented. The findings of this study support the integration of rapid administration protocols into clinical practice to achieve these benefits.

To fully realize the benefits of rapid rituximab administration in the short term, it is recommended that modifications should be made to the NHF catalogue to include corrective indicators that increase the valuation of services of services provided using rapid rituximab infusions. Additionally, public procurement criteria should incorporate rapid administration as a selection criterion to encourage its adoption.

Long-term changes in healthcare organization should focus on the development of outpatient care outside the hospital, which will reduce administrative burdens and relieve hospital resources. Shifting the administration of rituximab to outpatient clinics will not only ease the workload of staff directly involved in administering the drug but also reduce the administrative tasks associated with patient hospitalization. Currently, there is an ongoing discussion about systemic and legislative changes that would enable the implementation of drug programs exclusively in outpatient clinics. Considering the study findings and the benefits based on HB-HTA for rituximab, policymakers should consider organizational changes towards increasing the role of outpatient clinics in the long term.

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CONFLICT OF INTEREST STATEMENT
M. Czech and K. Giannopoulos - participation in advisory meetings with Sandoz. M Czech has received a honorarium for a lecture from Sandoz (2023). M. Sobierska is a Sandoz employee. J. Wieczorek, M. Mikułowska and B. Falkiewicz are employees of IQVIA. The funding source, Sandoz, supported the preparation and approved the study design. The funding source had no effect on the data collection, analysis, interpretation, writing of the report, and the decision to submit the article for publication.

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