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ORIGINAL RESEARCH

Economic Consequences of Administering Obinutuzumab as a Short Duration Infusion in Italian Patients with Advanced Follicular Lymphoma: A Cost Analysis

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ABSTRACT

OBJECTIVE: To assess time- and cost-savings in relation to active time of health care professional (HCP) and resource consumption of administering obinutuzumab as a short duration infusion (SDI) in patients in treatment for Follicular Lymphoma (FL).

METHODS: A cost-minimization model was developed to compare resource consumption and cost of the obinutuzumab SDI relative to obinutuzumab regular infusion rate (RIR) for the previously untreated and rituximab-refractory FL. Monetary valuation of resource and time allocated to treatment as a whole was carried out from the Italian Hospital and the societal perspective. Direct costs included HCP costs for drug preparation and administration activities, non-drug consumable costs, drug acquisition costs, and formal care costs. Indirect costs included the lost productivity of patients and informal caregivers. All costs (updated to 2021-value) were estimated by multiplying resource use by the unit cost of each resource. Evidence on resource use and unit costs were retrieved from scientific literature and standard Italian tariffs. A deterministic sensitivity analysis was used to test the results.

RESULTS: The administration time of obinutuzumab SDI is shorter than with obinutuzumab RIR, with a difference of 102 minutes per patient and for every cycle of administration beyond the first one. On average, the cost of HCP time invested in the preparation and administration of obinutuzumab RIR is € 92 during cycle 2 and from cycle 2 onwards, compared to € 54 per cycle of obinutuzumab SDI. Overall, the cost from the societal perspective is estimated to be € 38,698 for obinutuzumab RIR and € 37,692 for obinutuzumab SDI, resulting in a cost-saving per patient of € 1,007 (2.6%).

CONCLUSIONS: The application of obinutuzumab SDI schedule allows substantial reduction of hospital stay, improving quality of life of patient and caregiver and reducing costs and health care system burden. The time-savings with obinutuzumab SDI may improve clinical unit capacity by optimizing chair utilization and/or allowing rearrangements of the nurse residual time into valuable supplementary activities, spanning from more patient-centered clinical support to research and learning activity.

Keywords

Economic Evaluation; Oncology; Social Cost; Hospital Cost

INTRODUCTION

Follicular lymphoma (FL) is one of the most common lymphomas representing about 12-19% of all non-Hodgkin lymphomas (NHL) [1,2]. In Italy, the rate of new cases of FL is equal to 2.85 (95% CI: 2.78-2.92) per 100,000 person/year: its incidence increases with age—FL mainly affects adults over the age of 60, for which annual standardized incidence is up to 6.32 in people older than 65 years—with no differences between men (2.80) and women (2.90) [3]. FL is an indolent disease often diagnosed in an asymptomatic phase, for which initial observation (watch and wait approach) is recommended [2,4,5]. However, virtually all

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patients eventually progress to an active phase of disease requiring therapy, in most cases associated with favorable prognosis, but with considerable clinical heterogeneity and molecular and morphologic diversity. In particular, older age and more advanced stage, at the time of diagnosis, are associated with increased mortality rates [6-8].

Clinical course of the disease and patients' conditions lead the choice of systemic treatment, usually defined by using *Groupe d'Etude des Lymphomes Folliculaires* (GELF) criteria [4-6,9-12]. A rituximab-based approach of chemo-immunotherapy followed by rituximab maintenance has represented the gold standard of treatment and has dramatically improved response rates and overall survival (OS) [5,11]. Nevertheless, novel agents have recently filled in the therapeutic landscape, such as obinutuzumab, a humanized monoclonal CD20-directed antibody [13]. Obinutuzumab-based chemotherapy is an effective treatment for patients with previously untreated advanced FL and in patients with FL who did not respond or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen. It is approved for use in these populations in Italy. Its efficacy and safety profile for the treatment of untreated and rituximab-refractory FL patients were previously evaluated and described in phase III trials [14,15]. In addition, obinutuzumab-based chemotherapy resulted in longer progression-free survival than rituximab-based chemotherapy in first-line treatment of patients with advanced FL at intermediate or high risk of progression and is considered a cost-effective option in Italy [16].

Obinutuzumab is administered intravenously under physician supervision and in a hospital environment where resuscitation facilities are immediately available. Based on the prescribing information (SmPC), at cycle 1, it should be administered at 50 mg/h that may be escalated provided that the patient can tolerate it. Recently, according to evidence emerged in the GAZELLE trial (NCT03817853), the European Medicine Agency (EMA) approved a short duration infusion (SDI) (approximately 90 minutes of infusion time, achievable through an infusion rate up to 900 mg/h) from cycle 2 onwards, in patients who do not experience Grade ≥3 infusion related reactions (IRRs) during cycle 1 [17].

According to data derived from the GAZELLE study, we evaluated time- and cost-savings in relation to active time of health care professionals (HCPs) and resource consumption of administering obinutuzumab as a short duration infusion during cycle 2 and from cycle 2 onwards in combination with chemotherapy in patients in treatment for FL who do not experience any Grade ≥3 IRRs during the first cycle. The aim of this analysis is to provide a monetary valuation of resource and time allocated to treatment that can be saved through the short duration infusion of obinutuzumab from the Italian Hospital and the societal perspective.

METHODS

Model description

This analysis compares resource consumption and cost of obinutuzumab SDI relative to obinutuzumab regular infusion rate (RIR) for the previously untreated and rituximab-refractory FL. The cost analysis was carried out through a cost-minimization model developed in Microsoft Excel®. The logical flow of the model may be summarized in few steps:

- Identification of the population and its demographic and anthropometric characteristics (age, sex, and body weight);
- Identification of pharmaceutical consumption (i.e., dose and treatment duration) and acquisition costs;
- Identification of resource consumption and costs associated with in-hospital activities for IV administration;
- Comparison of resource consumptions and costs between obinutuzumab SDI and RIR.

The in-hospital IV administration process consists of four major phases: i) patient arrival; ii) drug preparation; iii) drug administration; and iv) patient commute. Each phase is associated with specific activities and sub-activities that are carried out by health care professionals. This approach allows to estimate costs directly accounting for healthcare resources (e.g., personnel, drug, non-drug consumable) consumed and the time spent with each resource as a patient moves along the care process.

The model supports both bottom-up (micro-costing) costing health care approach for allowing an analysis focused on the hospital perspective, and loss of patient- and caregiver-time to focus on societal perspective. Activities, sub-activities, HCPs, non-drug consumables used for in-hospital IV administration process were identified according to published cohort studies (Table I) [18-20].

Phase	Activity	Resource detail
Patient arrival	• Patient arrives and secretary receives the patient • Patient is accompanied to the treatment room	• Time-related to patient, caregiver, secretary, and hospital porter
Drug preparation	• Order prescription • Pre-check of prescription by pharmacist • Preparation of medicine tray and alcohol wipe down of items • Medicine preparation, or reconstitution & compounding • Double check of final preparation	• Time-related to pharmacist and pharmacy technician • Cost of non-drug consumables (pre-cleaning of LAF, post-cleaning of LAF, IV preparation consumables, IV compounding consumables
Drug administration	• CNS prepares the patient (weighs, cannulation, etc.) • Nurse double-checks the medicine • CNS prepares the tray and prepares herself • Drug is administered • Dialogue with nurse and termination • Possible observation time	• Time-related to CNS and staff nurse, patient and caregiver • IV administration consumables
Patient commute	• Patient commutes to the hospital • Patient commutes back home	• Time-related to patient and caregiver

Table I. *Summary of phases, activities and sub-activities, and details about in-hospital IV administration process*
LAF = Laminar Air Flow; CNS = Clinical Nurse Specialist; IV = Intravenous

Phase	Activity	Resource	Cycle 1/ Day 1	Cycle 1/ Day 8 and 15	Cycles 2-6 or 2-8 and maintenance
Patient commute	Patient commutes to the hospital (min)	Patient	30	30	30
		Caregiver	30	30	30
Patient arrival	Reception (min)	Secretary	1	1	1
		Receptionist	5	5	5
		Patient	6	6	6
		Caregiver	6	6	6
	Waiting time (min)	Patient	3	3	3
		Caregiver	3	3	3
	Patient is accompanied to the Tx room (min)	Hospital porter	1	1	1
		Patient	1	1	1
		Caregiver	1	1	1
Drug preparation	Pre-check of prescription (min)	Pharmacist	2	2	2
	Preparation of medicine tray and alcohol wipe down of items (min)	Pharmacy technician	3	3	3
	Medicine preparation, or reconstitution & compounding (min)	Pharmacy technician	16	16	16
	Double check of final preparation (min)	Pharmacist	2	2	2
	Not specified (n)	Pre-cleaning of LAF	1	1	1
		Post-cleaning of LAF	1	1	1
		IV preparation consumables	1	1	1
		IV compounding consumables	1	1	1
Drug administration	CNS prepares the patient (min)	CNS	5	5	5
	Nurse double-checks the medicine (min)	CNS	1	1	1
	CNS prepares the tray and prepares herself (min)	CNS	12	12	12
	Drug is administered (min)	CNS	255	195	195
	Dialogue with nurse and termination (min)	CNS	3	3	3
	Preparation patient (min)	Patient	21	21	21
		Caregiver	21	21	21
	Drug is administered (min)	Patient	255	195	195
		Caregiver	255	195	195
	Not specified (n)	IV administration consumables	1	1	1
	Possible observation time (min)	CNS	0	0	0
		Patient	0	0	0
		Caregiver	0	0	0
Patient commute	Patient commutes back home (min)	Patient	30	30	30
		Caregiver	30	30	30

Table II. *Time for activities, categorized by HCP, and quantity of non-drug consumables in obinutuzumab RIR (all cycles)*
LAF = Laminar Air Flow; CNS = Clinical Nurse Specialist; Tx: Treatment; IV: Intravenous

Phase	Activity	Resource	Cycle 1/Day 1	Cycle 1/ Day 8 and 15	Cycles 2–6 or 2–8 and maintenance
Patient commute	Patient commutes to the hospital (min)	Patient	30	30	30
		Caregiver	30	30	30
Patient arrival	Reception (min)	Secretary	1	1	1
		Receptionist	5	5	5
		Patient	6	6	6
		Caregiver	6	6	6
	Waiting time (min)	Patient	3	3	3
		Caregiver	3	3	3
	Patient is accompanied to the Tx room (min)	Hospital porter	1	1	1
		Patient	1	1	1
		Caregiver	1	1	1
Drug preparation	Pre-check of prescription (min)	Pharmacist	2	2	2
	Preparation of medicine tray and alcohol wipe down of items (min)	Pharmacy technician	3	3	3
	Medicine preparation, or reconstitution & compounding (min)	Pharmacy technician	16	16	16
	Double check of final preparation (min)	Pharmacist	2	2	2
	Not specified (n)	Pre-cleaning of LAF	1	1	1
		Post-cleaning of LAF	1	1	1
		IV preparation consumables	1	1	1
		IV compounding consumables	1	1	1
Drug administration	CNS prepares the patient (min)	CNS	5	5	5
	Nurse double-checks the medicine (min)	CNS	1	1	1
	CNS prepares the tray and prepares herself (min)	CNS	12	12	12
	Drug is administered (min)	CNS	255	195	93
	Dialogue with nurse and termination (min)	CNS	3	3	3
	Preparation patient (min)	Patient	21	21	21
		Caregiver	21	21	21
	Drug is administered (min)	Patient	255	195	93
		Caregiver	255	195	93
	Not specified (n)	IV administration consumables	1	1	1
	Possible observation time (min)	CNS	0	0	0
		Patient	0	0	0
		Caregiver	0	0	0
Patient commute	Patient commutes back home (min)	Patient	30	30	30
		Caregiver	30	30	30

Table III. *Time for activities, categorized by HCP, and quantity of non-drug consumables in obinutuzumab SDI (all cycles)*
LAF = Laminar Air Flow; CNS = Clinical Nurse Specialist; Tx = Treatment; IV = Intravenous

Population and inputs

Demographic characteristic and anthropometric measures of patients enrolled in the GAZELLE trial were assumed as a proxy of Italian patients with FL [17].

Direct and indirect costs were used according to the perspective adopted. When the cost-analysis was run from hospital perspective, only direct medical costs referring to the cost of resources to provide treatment—i.e., drug, non-drug consumables, hospital overheads, HCPs time—were accounted for. When the perspective was from society's point of view, direct non-health care costs referring to formal and informal care, and indirect costs due to the patient time lost to treatment were calculated. In general, each direct and indirect cost was calculated by multiplying the estimated resource use by its associated unit cost. In Table II and Table III, the list of patient-related activities and tasks associated with the IV administration of obinutuzumab RIR and SDI are summarized [18-20].

Direct health care costs

Ex-factory net price with confidential rebates was used for obinutuzumab 1,000 mg (€ 1,659.56). Obinutuzumab is administered during the induction phase for six/eight cycles in combination with chemotherapy [13]. Duration of the induction phase that depends on the concomitant chemotherapeutic agent was weighted according to their frequency of use

Cycle	Regular infusion rate (RIR)			Short duration infusion rate (SDI)		
	Cycle 1		Cycles 2–6 or 2–8 and maintenance	Cycle 1		Cycles 2–6 or 2–8 and maintenance
	Day 1	Day 8 and 15	Day 1	Day 1	Day 8 and 15	Day 1
mg/h	50	100	100	50	100	100
mg/h increments every 30'	50	100	100	50	100	900
mg/h maximum rate	400	400	400	400	400	900
Dose per day (mg)	1,000	1,000	1,000	1,000	1,000	1,000
Time (min)	255	195	195	255	195	93

Table IV. *Administration schedule and administration rate both obinutuzumab RIR and SDI*

observed in literature [14]. Patients with at least partial response to induction treatment continued to receive obinutuzumab 1,000 mg as single-agent maintenance therapy every 2 months for 2 years (12-cycle)—more details on administration schedule and administration rate both obinutuzumab SDI and RIR are shown in Table IV [13].

Time for the activities and sub-activities, categorized by HCP, was valued by average hourly gross wages, as defined within HCP collective labor agreement (Table V) [21].

All non-drug consumables for preparation and administration of in-hospital IV therapies were identified in the literature and their costs were set as per specific public tender price (Table VI) [19,20]. The overhead costs, not directly related to consumables or HCPs activities, were considered, and valued according to an Italian survey: in particular, these costs were estimated as the 20% of full costs of health service—i.e., in-hospital IV administration, but excluding drug acquisition cost [23].

Personnel	Hourly cost (€/h)	Source
Pharmacist	33.18	Aran, 2018 [21]
Pharmacy technician	17.92	Aran, 2018 [21]
Clinical Nurse Specialist	18.00	Aran, 2018 [21]
Hospital porter	15.64	Aran, 2018 [21]
Receptionist	14.31	Aran, 2018 [21]
Secretary	15.07	Aran, 2018 [21]
Patient	5.91	Elaboration from [26-29]
Caregiver[1]	4.42	Elaboration from [26-29]

Table V. *Patient, caregiver, and health care professional hourly cost*
[1] Caregiver costs is a weighted mean that takes into account distribution of formal and informal care

Non-drug consumable description	Total cost (€) – *una tantum*
Pre-cleaning of LAF	0.24
Post-cleaning of LAF	0.24
IV preparation consumables	10.54
IV compounding consumables	3.42
IV administration consumables	10.75

Table VI. *Non-drug consumable cost (for details on quality and quantity resource, please to refer O'Brien et al. [19])*
LAF = Laminar Air Flow

Direct non-health care and indirect costs

Indirect costs referred to patient were estimated as productivity loss, using the human capital approach and the Proxy Good approach for paid and unpaid productivity losses, respectively (Table V) [24,25].

The productivity losses, which occurred both in paid and in unpaid work, due to IV administration are proportionally subtracted from daily routine based on Italian Time Use Survey (TUS) of ISTAT—i.e., TUS provides data, grouping by age and sex, on time dedicated to paid and unpaid activities of the general population [26]. Thus, the hours per day dedicated to paid activities were valued through the Italian average hourly gross wage; for what concerns unpaid production, which includes household work, caring for oneself, family member or others, and volunteer work, in order to give a monetary value, a minimum wage for domestic worker, formal caregiver and volunteering was used [27-29].

Societal costs were integrated with costs accrued by the caregiver: 80% of patients are accompanied during in-hospital IV administration, and 3 out of 4 times it's a family member (Table V) [30].

Formal care cost was based on the basic wage of domestic workers, as defined within the National Collective Bargaining Agreement for Domestic Workers (Table V) [28]. In order to give a monetary value to informal care, the time dedicated to caring was proportionally subtracted from daily routine of paid and unpaid activities based on Italian TUS [26]. Demographics of caregivers were collected from Italian survey [30].

Phase	Induction (min)		Maintenance (min)[3]
	Cycle 1[1]	Cycle 2-6/2-8[2]	
Obinutuzumab RIR			
Patient arrival	21	43	84
Drug preparation	67	135	267
Drug administration	708	1,316	2,590
Patient commute	180	366	720
Total	**975**	**1,860**	**3,661**
Obinutuzumab SDI			
Patient arrival	21	43	84
Drug preparation	67	135	267
Drug administration	708	696	1,370
Patient commute	180	366	720
Total	**975**	**1,240**	**2,441**

Table VII. *Total time (min) per each phase (induction: Cycle 1 and Cycle 2-6/2-8; and maintenance) in case of administration of obinutuzumab as RIR and SDI (per patient)*
[1] One administration on days 1, 8 and 15
[2] One administration on day 1 every 21 days (duration of the induction phase that depends on the concomitant chemotherapeutic agent is weighted according to their frequency of use observed in GALLIUM study [14]
[3] One administration on day 1 every two months for two years (max 12 administrations)
RIR = Regular Infusion Rate; SDI = Short Duration Infusion

Sensitivity analysis

Uncertainties of input parameters, and their effect on estimated result, was explored through a deterministic sensitivity analysis (DSA). The input parameters were varied (one by one while all other variables were held at baseline values) ± 20% of the base case.

This allows to test the sensitivity/risk associated with one uncertainty/variable [31].

Results—i.e., incremental costs of obinutuzumab SDI vs. RIR—are presented using a tornado diagram, where the data categories are listed vertically instead of the standard horizontal presentation, and the categories are ordered so that the largest bar appears at the top of the chart. The top bars would represent the items that contribute the most to the variability of the outcome, and therefore what the decision maker should focus on.

RESULTS

Base case

The overall therapy administration time of obinutuzumab is shorter for SDI compared to RIR: the average time difference is 102 min for every cycle of administration beyond the first one, while for a complete treatment, the resulting average time saving is 1,800 min (i.e., 30 h) per patient (Table VII).

	Cycle 1	Cycle 2-6/2-8	Maintenance
Obinutuzumab RIR			
Drug (€)	4,978.68	1,659.56	1,659.56
HCP (€)	299.94	92.48	92.48
Non-drug consumables (€)	94.46	31.49	31.49
Patient and caregiver (€)	157.74	49.14	49.14
Total (€)	**5,530.82**	**1,832.66**	**1,832.66**
Obinutuzumab SDI			
Drug (€)	4,978.68	1,659.56	1,659.56
HCP (€)	299.94	54.36	54.36
Non-drug consumables (€)	94.46	31.49	31.49
Patient and caregiver (€)	157.74	31.63	31.63
Total (€)	**5,530.82**	**1,777.04**	**1,777.04**

Table VIII. *Total costs of administering obinutuzumab as RIR and SDI per cycle (per patient)*
HCP = Healthcare Professional; RIR = Regular Infusion Rate; SDI = Short Duration Infusion

On average, the cost of HCP time invested in the preparation and administration of obinutuzumab RIR is € 92 during cycle 2 and from cycle 2 onwards, compared to € 54 per cycle of obinutuzumab SDI. For a complete treatment—it includes the induction phase for six/eight cycles, which depends on the concomitant chemotherapeutic agent, and 12 cycles of maintenance phase—this would result in a cost of € 1,974 for obinutuzumab RIR and € 1,284 for obinutuzumab SDI, with a cost differential of € 690 per patient. The clinical nurse is the HCP type that gets the most advantage from obinutuzumab SDI, both in terms of time allocated to treatment and cost savings. The resource utilization of pharmaceuticals, per health care resources and commute to and from the hospital are

	Obinutuzumab RIR	Obinutuzumab SDI	Difference	Relative difference
Drug (€)	35,013.40	35,013.40	0.00	0.0%
HCP(€)	1,973.63	1,283.73	-689.90	-35.0%
Non-drug consumables (€)	664.32	664.32	0.00	0.0%
Patient and caregiver (€)	1,047.03	730.23	-316.80	-30.3%
Total (€)	38,698.37	37,691.67	-1,006.70	-2.6%

Table IX. *Cost difference per patient-therapy cost (obinutuzumab SDI vs. RIR)*
HCP = Healthcare Professional; RIR = Regular Infusion Rate; SDI = Short Duration Infusion

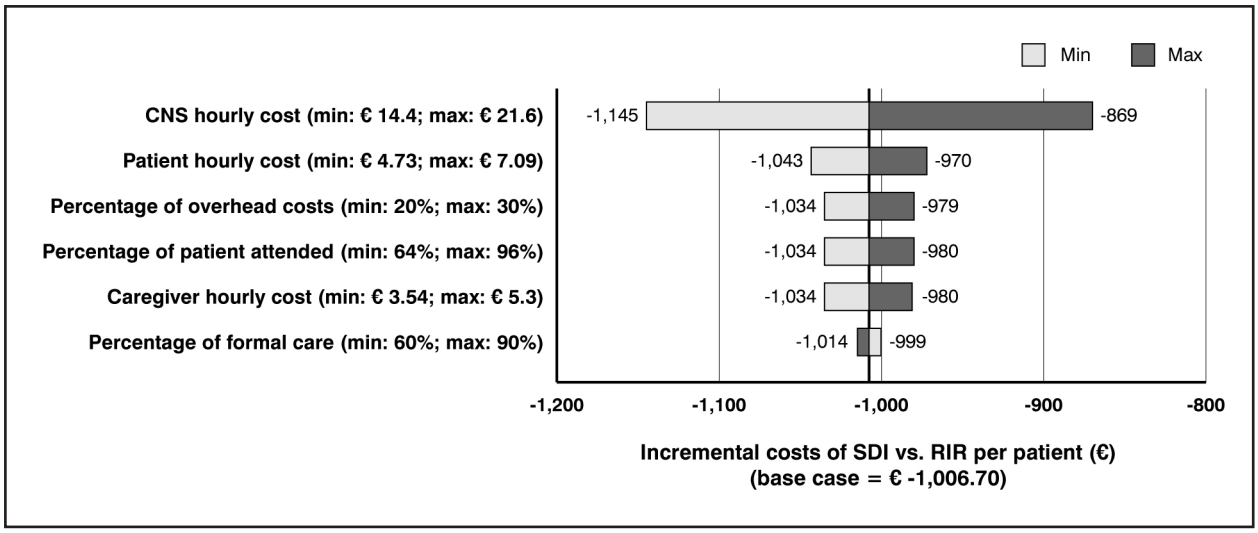

Figure 1. *Tornado diagram for sensitivity analysis*
CNS = Clinical Nurse Specialist; RIR = Regular Infusion Rate; SDI = Short Duration Infusion

presented in Table VIII. The time allocated to obinutuzumab treatment, both by patients and their relatives, are presented in Table VII.

The cost from the societal perspective is estimated to be € 38,698 for obinutuzumab RIR and € 37,692 for obinutuzumab SDI, resulting in a cost-saving of € 1,007 (2.6%) (Table IX). Direct medical costs from hospital/health care provider point-of-view represent 69% of overall cost difference resulting from the comparison between obinutuzumab SDI vs. obinutuzumab RIR, while 31% is due to caregiving and patient costs.

Sensitivity analysis

Results of DSA are illustrated in Figure 1. The incremental costs are most strongly influenced by Clinical Nurse Specialist hourly cost; however even under the most extreme cases tested (between € 14-22 per hour), obinutuzumab SDI remains a favorable alternative.

DISCUSSION

The presented analysis on previously untreated and rituximab-refractory FL patients compares resource consumption in terms of costs and time allocated to treatment of administering obinutuzumab as a short duration infusion and obinutuzumab regular infusion rate both in combination with chemotherapy.

According to our analysis, obinutuzumab SDI is less costly both from the hospital perspective (€ 37,651 for obinutuzumab RIR vs € 36,961 for obinutuzumab SDI with a relative difference of 1.8%) and from the societal perspective (€ 38,698 for obinutuzumab RIR vs € 37,692 for obinutuzumab SDI with a relative difference of 2.6%). It allows to save, from cycle 2 onwards, HCP time during the IV administration, corresponding to 1h42' per cycle administered (3h36' for obinutuzumab RIR vs 1h54' for obinutuzumab SDI).

From the hospital perspective, these findings may represent an additional opportunity: HCP time-savings may both decrease the workload and improve the resource allocation for increasing the quality of health care services. In particular, HCP time-savings allow to treat, on average, 2 more patients per day for each chair available for IV administration with obinu-

tuzumab—assuming 8-hours in a workday. Alternatively, through a resource optimization process, obinutuzumab SDI allows to free an average of half a workday that may be allocated to new activities.

Also, the societal costs of caregiver and patient potentially play a key role in the decision-making processes, and, historically, the societal perspective has frequently been recommended [32]. In the present analysis, obinutuzumab SDI contributes to a reduction of 30% of the societal costs of caregiver and patient relative to obinutuzumab RIR in the treatment of FL patients.

Some limitations and assumptions of the present analysis are worthwhile mentioning. In the absence of a specific time & motion study that collected data on the resource consumption and the time for each activity concerning the preparation and administration of obinutuzumab, we assumed this would reflect what has already been published for other infusion therapies. The total therapy costs do not include resource consumption for the chemotherapy which is administered in combination during induction phase; premedication, which is recommended for patients with FL, and costs referred to implantation, removal, maintenance, and complication management of the central venous access devices. These costs, however, are not differential. Further minor limitation is due to the need of assuming demographic characteristic and anthropometric measures of patients from the GAZELLE trial, which enrolled only previously untreated FL patients to evaluate the safety of administering obinutuzumab SDI [17]. Nevertheless, there is no reason to think that rituximab-refractory patient—for which obinutuzumab SDI may be also administered—could have different demographic and anthropometric characteristic measures from those of untreated patient, since resistance to rituximab generally must be assessed within 6 months from the start of frontline therapy.

As demonstrated in the phase IV GAZELLE study, the safety and the efficacy of obinutuzumab have been shown to be preserved when the agent is administered at 90-minute SDI from Cycle 2 [17]. Specifically, no patients reported grade 3 or higher infusion-related reactions during cycle 2 of treatment with the short-duration infusion, and no unusual safety signals occurred. Based on these findings, regulatory agencies have approved a shorter, 90-minute infusion time for obinutuzumab to be given in combination with chemotherapy in patients with previously treated or untreated advanced follicular lymphoma.

From the hospital point of view, the reduction of infusion time represents a valuable opportunity for rearrangements of clinical logistics. For instance, the nurse residual time could be invested into supplementary activities that span from more patient-centered clinical support to research and learning activity. In particular, clinical nurse's extra clinical time should be taken to boost patient's and caregiver's quality of care through psychological and non-clinical activities. On the other hand, from the patient's perspective, reduced infusion time equals shorter hospital stays, with longer time spent outside the hospital to daily life activities, with predictable improvement of patient's and caregiver's quality of life. Furthermore, the shorter time infusion could also steer an improvement of patients' compliance to therapy and potentially ward off hospitalization anxiety. The improvement of the experience of care becomes even more meaningful for those patients who have to face long distances to get to the treatment center: infusion time-savings could mitigate logistic inconvenience both for patient and for caregiver (e.g., overnight accommodation and related additional costs).

An exploratory investigator analysis was completed during the GAZELLE study to evaluate the site experience with the SDI and standard infusions of Obinutuzumab [33]. Provider-reported outcomes—from one hundred attendee-interviews that were collected using a questionnaire—report as obinutuzumab SDI minimizes patient treatment burden with little or no impact on health-related quality of life, and was preferred by health-care providers for the time savings, convenience, and patient comfort. In particular, 60% of clinical nurse specialists and physicians reported that SDI would be able to save at least 2 hours in infusion time per visit, and 65% indicated SDI as much more convenient versus standard infusion. Overall, 95% of participants preferred obinutuzumab SDI over standard infusion for reasons attributed to time savings and patient treatment burden.

Consequently, obinutuzumab SDI has a favorable economic value for Italy, which, however, is not transferable to other countries, due to the specificity of the cost sources used. Even so, the advantage of obinutuzumab SDI in terms of resource-savings may be generalized and replicable to other countries. In particular, the allocation time of HCPs to other activities is of greater impact in non-OECD countries, where health expenditure is increasing, but where a lack of economic resources and available HCP persists [34-37].

CONCLUSION

Obinutuzumab offers improved PFS for patients with previously untreated advanced and rituximab-refractory follicular lymphoma. Usually, the standard infusion time for obinutuzumab in this patient population is 3 to 4 hours. Results from the open-label, phase 4 GAZELLE trial suggest that 90-minute SDI may be as effective, without increasing the rate of adverse events. The consequent approval by regulatory bodies of this schedule allows substantial reduction of hospital stay, improving quality of life and reducing health care system burden. The latter is of major importance given the continuous increased complexity of providing modern healthcare to hematological patients, often in the context of heavily overloaded clinical units. To conclude, obinutuzumab administered as a short duration infusion, shorter than regular infusion rate in Italian patients with advanced FL leads to favorable economic consequences, with a cost-saving around one thousand Euro from the perspective of society. Moreover, the time-savings with obinutuzumab SDI may improve clinical unit capacity by optimizing chair utilization and/or allowing rearrangements of the nurse residual time into valuable supplementary activities, spanning from more patient-centered clinical support to research and learning activity.

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