

ECONOMIC CONSEQUENCES OF ADMINISTERING OBINUTUZUMAB AS A SHORT DURATION INFUSION IN ITALIAN PATIENTS WITH ADVANCED FOLLICULAR LYMPHOMA: A COST ANALYSIS

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Objective

- Follicular lymphoma (FL) represents 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 (IC 95%: 2.78-2.92) per 100,000 person/year.^[3]
- 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.^[4, 5]
- It is administered intravenously under physician supervision and in hospital environment. 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 without Grade ≥3 infusion related reactions (IRRs) during cycle 1.^[6]
- The present analysis assesses time- and cost-savings in relation to active time of health care professional (HCP) and resource consumption of administering obinutuzumab as SDI in patients in treatment for FL.
- Monetary valuation of resource and time allocated to whole treatment was carried out from the Italian Hospital and the societal perspective.

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.
- The in-hospital IV administration process consists of four major phases: (1) Patient arrival, (2) Drug preparation, (3) Drug administration and (4) Patient commute. Each phase is associated with specific activities and sub-activities, which are carried out by HCPs, and non-drug consumables used for in-hospital IV administration process (Table 1).^[7, 8, 9]
- Direct costs include HCP costs for drug preparation and administration activities, non-drug consumable costs, drug acquisition costs, and formal care costs. Indirect costs include 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. Net prices for drugs with confidential rebates were used (confidential discounts).^[20]
- Evidence on resource use and unit costs were retrieved from scientific literature and standard Italian tariffs. In particular:
 - 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 1).^[7, 8, 9, 10]
 - All non-drug consumables for preparation and administration of in-hospital IV therapies were identified in the literature and their cost was set as per specific public tender price (Table 1).^[8, 11]
 - 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 1).^[12, 13]
 - 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 1).^[18] Formal care cost was based on the basic wage of domestic workers, as defined within the National Collective Bargaining Agreement for Domestic Workers (Table 1).^[16] 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.^[14] Demographics of caregivers were collected from Italian survey.^[18]

Table 1. Costs

Cost item	Value	Source	Drug administration routine	
Categories				
Pharmacist	33.18 €	10	Obinutuzumab is administered during the induction phase for six/eight cycles in combination with chemotherapy. Patients with at least partial response receive obinutuzumab 1,000 mg as single-agent maintenance therapy every 2 months for 2 years (12-cycle). ^[4, 5]	
Pharmacy technician	17.92 €	10		
Clinical Nurse Specialist (CNS)	18.00 €	10		
Hospital porter	15.64 €	10		
Receptionist	14.31 €	10		
Secretary	15.07 €	10		
Patient	5.91 €	14, 15, 16, 17		
Caregiver	4.42 €	14, 15, 16, 17		
Drug and non-drug consumables				
Obinutuzumab 1,000 mg *	2,828.63	19		
Non-drug consumables (preparation and compounding)	14.44 €	8, 11		
Non-drug consumables (administration)	10.75 €	8, 11		

How to manage productivity loss
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.^[14]

* Ex-factory price net of mandatory discounts is shown. For drug cost, confidential discounts were applied.^[20]

Results

- Administration time of obinutuzumab SDI is shorter than obinutuzumab RIR (Table 2), 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 preparation and administration of obinutuzumab RIR is €92 during cycle 2 and beyond, while €54 for cycle of obinutuzumab SDI.
- Overall, the cost from the societal perspective is €38,698 for obinutuzumab RIR and €37,692 for obinutuzumab SDI, resulting in a cost-saving per patient of €1,007 (2.6%) (Table 3).
- Total savings is mainly affected by CNS cost (Figure 1).

Table 2. Total time (min) per each phase in case of administration of obinutuzumab as RIR and SDI (per patient)

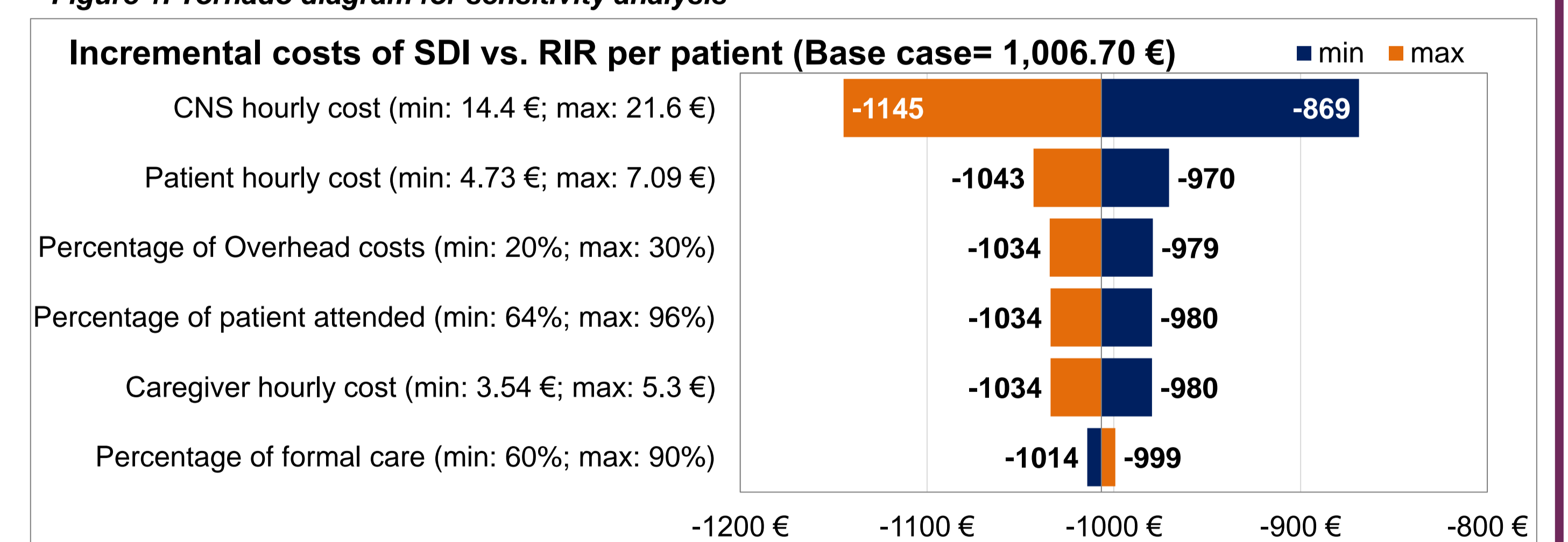
Phase	Induction		Maintenance
	Cycle 1	Cycle 2-6/2-8	
Obinutuzumab RIR			
Patient arrival	21'	43'	84'
Drug preparation	67'	135'	267'
Drug administration	708'	1,316'	2,590'
Patient commute	180'	366'	720'
Total	975'	1,860'	3,661'
Obinutuzumab SDI			
Patient arrival	21'	43'	84'
Drug preparation	67'	135'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

In the 1st cycle, one administration on days 1, 8 and 15; Cycle 2-6/2-8: 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);^[4] Maintenance: one administration on day 1 every two months for two years (max 12 administrations)

Table 3. Cost difference per patient-therapy cost (obinutuzumab SDI vs. RIR)

	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%

Figure 1. Tornado diagram for sensitivity analysis



Conclusions

- Obinutuzumab SDI allows reduction of hospital stay, improving quality of care of patient and caregiver and reducing healthcare 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.
- Hypothetically, HCP time-savings allow to treat, on average, 2 more patients per day for each chair available for IV administration with obinutuzumab – 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.

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