Feasibility Evaluation for a Rituximab Utilization Study to be Conducted in Infusion Centers

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CONFLICT OF INTEREST STATEMENT

The project was funded by Roche/Genentech. Iain Tatt and Pavel Napalkov are employees and shareholders of F. Hoffmann-La Roche Ltd. RTI Health Solutions employees work on projects funded by pharmaceutical companies, including manufacturers of treatments for patients with autoimmune diseases. Elizabeth Andrews, Manel Pladevall, and Susana Perez-Gutthann, as employees of RTI Health Solutions, participate in project advisory boards funded by pharmaceutical companies, including Roche/Genentech.

BACKGROUND

- Automated clinical databases (i.e., hospital or population prescription databases) are an important data source for drug utilization studies; however, often they do not capture prescriptions on a national level for drugs administered in infusion centers (ICs) (e.g., biological agents), and other data sources are required.
- A feasibility evaluation (FE) was conducted to inform the design of a drug utilization study and to evaluate the counseling practices for rituximab (RTX) at ICs. RTX is a biological agent approved for the treatment of rheumatoid arthritis (RA), granulomatosis with polyangiitis, and microscopic polyangiitis, which is administered in specialized ICs.
- The ICs that administer RTX are very diverse regarding type of site (e.g., academic vs. private small offices), specialty of physicians running the sites (e.g., internal medicine vs. rheumatology), and patient case-mix (e.g., majority RA patients vs. majority other autoimmune diseases) across the different countries and health systems in Europe.
- There is some evidence of RTX use in additional conditions (e.g., systemic lupus erythematosus), but the extent of this use is unclear.

OBJECTIVE

- The FE was performed to determine if a single study conducted in ICs across five European countries (France, Germany, Italy, Spain, and the UK) could be implemented to characterize clinical use of RTX via medical record abstraction and evaluate RTX counseling practices via patient questionnaire.

Feasibility Goals

1. Evaluate characteristics of sites where patients are treated
2. Obtain estimates of the number of patients treated with RTX by clinical indication to confirm study size and determine number of ICs required per country
3. Obtain input on IC counseling practices and patient flow to determine if the patient survey could be conducted at the site prior to the provision of new counseling on educational materials and to evaluate how to minimize impact on day-to-day activities
4. Assess whether IC records provide the patient disease information needed for medical record abstraction and whether ICs have the resources to perform the abstraction
5. Assess the interest of ICs in participating in the research study

METHODS

Data Collection

- Interviews were conducted with sponsor local affiliates in each country to learn more about ICs' characteristics and RTX prescribing and use patterns.
- A feasibility questionnaire was developed to be completed by the ICs' principal investigators or study coordinators. The questionnaire was offered in English, French, German, Italian, and Spanish and could be completed individually or through a telephone interview with a member of the study team. The questionnaire collected the following information: number of patients using RTX for nononcology conditions and the patient flow at the ICs, ICs' characteristics and operations, overall feasibility of implementing data collection at the ICs, and ICs' interest in participating in the future study.
- A clinical expert (national coordinator) was identified in each country to provide consultation and support the recruitment of ICs.
- ICs were primarily contacted by e-mail to participate in the FE; some follow-up was conducted by phone. Follow-up e-mails and calls were used to obtain missing data and/or clarify responses.
- Sixty-five sites were contacted for participation, and 30 completed the questionnaire (overall response rate, 46%; range by country, 22%-75%).

Table 1. Site Recruitment Summary

	France	Germany	Italy	Spain	UK
Sites contacted	10	10	23	12	10
Sites responded with interest	8	7	5	11	6
Questionnaires sent	8	7	5	11	6
Refusals	0	0	1	2	3
Nonrespondents	1	3	16	0	1
Questionnaires completed	6	5	5	9	5
Response rate[a]	67%	50%	22%	75%	50%

[a]Response rate equals the number of returned questionnaires divided by the number of sites contacted.

Data Management and Statistical Methods

- Each form was keyed one time by the interviewer. The same interviewer or a second person performed a quality control check. Inconsistencies in the database were resolved.
- Descriptive analyses were stratified by country. Summary tables included frequencies for categorical variables and means, medians, minimums, and maximums for continuous variables.

RESULTS

Feasibility Goal 1: Evaluate characteristics of sites where patients are treated

Table 2. IC Characteristics by Country

	Country				
	France (n = 6)	Germany (n = 5)	Italy (n = 5)	Spain (n = 9)	UK (n = 5)
Characteristic	n (%)	n (%)	n (%)	n (%)	n (%)
Affiliated with academic institution?					
Yes	6 (100)	4 (80)	3 (60)	8 (89)	4 (80)
No	0 (0)	1 (20)	2 (40)	1 (11)	1 (20)
What physician specialties are represented within the IC? Select all that apply					
Rheumatology	4 (67)	5 (100)	5 (100)	6 (67)	5 (100)
Oncology	0 (0)	2 (40)	1 (20)	2 (22)	0 (0)
Internal medicine	3 (50)	2 (40)	2 (40)	8 (89)	2 (40)
Neurology	1 (17)	1 (20)	1 (20)	3 (33)	0 (0)
Nephrology	0 (0)	1 (20)	1 (20)	3 (33)	2 (40)
Dermatology	1 (17)	1 (20)	1 (20)	3 (33)	2 (40)
Other	0 (0)	2 (40)	3 (60)	2 (22)	2 (40)
Combinations of responses to physician specialties					
Just rheumatology	2 (33)	1 (20)	2 (40)	1 (11)	1 (20)
Rheumatology + 1 other	1 (17)	1 (20)	1 (20)	1 (11)	1 (20)
Rheumatology + 2 others	1 (17)	1 (20)	1 (20)	1 (11)	2 (40)
Rheumatology + 3 or more others	0 (0)	2 (40)	1 (20)	3 (33)	1 (20)
Not rheumatology	2 (33)	0 (0)	0 (0)	3 (33)	0 (0)
Types of patients infused with RTX in the past year					
RA only	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
RA and other autoimmune diseases	5 (83)	4 (80)	5 (100)	5 (56)	5 (100)
Other autoimmune diseases only	1 (17)	0 (0)	0 (0)	4 (44)	0 (0)
Is the IC currently conducting other RTX research?					
Yes	2 (33)	3 (60)	1 (20)	2 (22)	1 (20)
No	4 (67)	2 (40)	4 (80)	7 (78)	4 (80)

Findings:

- The majority of ICs were affiliated with an academic institution; most represented a mix of specialties, with the two most common being rheumatology and internal medicine.
- The majority of ICs treated a mix of patients with RA and other autoimmune diseases.
- Many ICs did not have previous experience conducting RTX research.

Implication for study:

- This information will guide site selection in the future study to ensure a diverse representation of settings, research backgrounds, and physician/patient mixes.

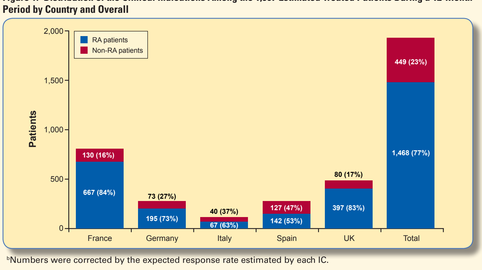
Feasibility Goal 2: Obtain estimates of the number of patients treated with RTX by clinical indication to confirm study size and determine number of ICs required per country

Table 3. Projected Patient Volume per IC and by Country for a Common 6-Month Period[a]

	France (n = 6)	Germany (n = 5)	Italy (n = 5)	Spain (n = 9)	UK (n = 5)
Number of eligible unique patients					
Mean	38	18	7	21	36
Median (range)	27 (7-120)	13 (3-40)	8 (2-10)	12 (6-60)	20 (18-60)
n	5	5	5	9	5
Number of patients infused[b]					
Mean	50	21	9	12	35
Median (range)	29 (7-116)	27 (3-40)	9 (8-11)	12 (2-18)	29 (16-70)
n	6	5	5	9	5

[a]Responses to both questions were imputed to a 6-month period to facilitate comparison. (In the original questionnaire, time frames were 12 months for the question on eligible patients and 3 months for the question on number of patients infused.)

Figure 1. Distribution of the Clinical Indications Among the 1,967 Estimated Treated Patients During a 12-Month Period by Country and Overall



[b]Numbers were corrected by the expected response rate estimated by each IC.

Findings:

- Average number of patients infused over a 6-month period across ICs ranged between 9 and 50. The average number of patients per IC is larger in France and the UK than in the other countries.
- Overall, 1,468 patients were reportedly treated for RA during a 12-month period and 449 patients for other autoimmune diseases (Figure 1).
- In Spain and Italy, clinical indication for other autoimmune diseases was more common, but sites that treat only patients with RA might have been underrepresented.

Implication for Study:

- A target sample size of 100 patients per country was deemed feasible, and the future study will include 10 to 15 ICs per country, each recruiting 7 to 10 patients to achieve this study size.

Feasibility Goal 3: Obtain input on IC counseling practices and patient flow to determine if the patient survey could be conducted at the site prior to the provision of new counseling on educational materials and to evaluate how to minimize impact on day-to-day activities

Table 4. Average Infusion Wait Times and Administration Times

	France (n = 6)	Germany (n = 5)	Italy (n = 5)	Spain (n = 9)	UK (n = 5)
Average infusion wait time (minutes)					
Mean	93	39	51	43	25
Median (range)	90 (60-210)	30 (20-60)	45 (30-90)	40 (10-90)	30 (0-45)
n	6	5	5	8	5
Average infusion time for RA (minutes)					
Mean	240	231	294	250	282
Median (range)	240 (210-300)	255 (120-300)	300 (240-360)	248 (120-360)	270 (180-450)
n	5	5	5	6	5
Average infusion time for other autoimmune diseases (minutes)					
Mean	270	214	344	240	278
Median (range)	240 (210-360)	218 (120-300)	300 (240-550)	240 (120-360)	240 (180-450)
n	5	4	5	9	4

Findings:

- The average wait time for a patient prior to receiving his or her RTX infusion varied by country, from a mean of 25 minutes in the UK to 93 minutes in France.
- Even with variability in wait times, there would be enough time to recruit patients for the future study and have them complete a brief patient questionnaire prior to receiving their RTX infusion.
- Average RTX infusion times for RA and other autoimmune diseases were consistent across all countries, an average of 259 minutes for RA and 266 minutes for other autoimmune diseases.

Table 5. Patient Counseling on RTX

	France (n = 6)	Germany (n = 5)	Italy (n = 5)	Spain (n = 9)	UK (n = 5)
How often is counseling on the potential risks associated with RTX provided to patients as part of their infusion visit?					
Don't know	0	0	0	0	0
Every time	2	0	1	4	3
Most of the times	1	2	1	0	0
Some of the times	2	1	0	1	1
Only the first time	1	2	3	4	1
Never	0	0	0	0	0
If counseling is given, at what point during the visit does the patient typically receive counseling about RTX?					
Before the infusion	6	5	5	9	5
During the infusion	0	0	0	0	0
After the infusion	0	0	0	0	0

Findings:

- There was variability across all ICs and countries on the frequency with which counseling on the potential risks associated with RTX is provided to patients. However, all ICs reported that if counseling is given, it is provided before the patient's infusion.
- Approximately 20% of the ICs' responses indicated that they may not have the ideal set-up to implement electronic data capture from a technology stand point.

Implications for Study:

- It was deemed feasible for the patient to complete a brief paper-based questionnaire at the IC before receiving RTX counseling or educational materials and before receiving their RTX infusion.

Feasibility Goal 4: Assess whether IC records provide the patient disease information needed for medical record abstraction and whether ICs have the resources to perform the abstraction

Findings:

- All ICs could access the patient medical records, either electronically or on paper.
- All ICs in France, Italy, and Spain reported that a health care professional on staff would be available to abstract medical records. One IC in Germany and two in the UK reported not having a staff member available.
- None of the ICs in France, Germany, or Italy saw any obstacles to completing the medical chart abstraction task. Two ICs in Spain expressed concern with having enough time to perform the task, and three ICs in the UK noted concerns with having available staff and time for this task.
- Most ICs reported availability of demographic, treatment, and disease information in patient medical records

Implications for Study:

- The medical record abstraction is feasible in all ICs; however, some ICs might require support to implement the medical record abstraction.

Feasibility Goal 5: Assess the interest of ICs in participating in the research study

Finding: All but one IC said they would be interested in participating in the study.

Implication for study: Sites that participated in the FE will be approached for participation in the future study, facilitating the overall site recruitment process.

LESSONS LEARNED

- Site participation is higher with active support from a local affiliate and national coordinator.
- Most countries responded well via e-mail; little phone follow-up was required.
- Content of returned questionnaires was mostly complete; some queries were required.
- It is feasible to conduct both the medical record abstraction and the patient questionnaire as components of the same future study.
- Results were valuable in confirming the study feasibility and in finalizing the study design and protocol.

CONCLUSION

- Drug utilization studies can be performed when usual data sources are not available, but FEs should be conducted to guide the study design and confirm feasibility, especially when the study is conducted in several countries with different health care systems and prescribing practices.

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