Different Willingness to Pay for Curative Therapies in France: A Cost per Cure Analysis of Medicines in Different Therapeutic Areas

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Dinh A [1], Henriksen A [2], Schey C[3], Lopes S[4]

1. Hôpital Raymond-Poincaré, 92380 Garches, France; 2. Shionogi BV, Medical Affairs Europe; 3. Global Market Access Solutions, Switzerland; 4. Shionogi BV, Global Market Access

Background

Traditionally, the willingness to pay (WTP) for medicines is evaluated through cost-effectiveness analyses, but these, although robust in their outcomes, are complex in their structures and data requirements. A cost per cure analysis is a simpler metric that considers the clinical benefits and economic costs of medicines for curative therapies, and provides insights of the WTP.

The increasing prevalence of antibiotic resistance and the associated risks to health are well documented [1,2]. The World Health Organization (WHO) list of pathogens, referred to as the critical priority pathogens for which new antibiotics are urgently needed[3], highlights this unmet medical need, and especially for Gram-negative infections. However, R&D in antimicrobial treatments has decreased in recent years [4]. By contrast, R&D in cancer drugs has grown substantially in the last 25 years, having quadrupled since 1996 and nearly doubled since 2008 alone, thereby contributing almost 40 percent of the global clinical pipeline [5].

Objectives

In this study, using the cost per cure metric, we aimed to understand the differences in observed WTP for recently approved branded curative pharmaceutical treatments in different therapeutic areas in France, with a focus on antibacterials, given the high priority antimicrobial resistance has in the healthcare policy agenda in France. We also sought to understand how the cost per cure varies across different therapeutic areas, and to ascertain other key drivers that affect this metric.

Methods

A stepwise process was used to assess the cost per cure per licensed therapeutic indication in France for adult treatments:

- "Cure" was defined as the eradication or resolution of the condition in patients, after permanent discontinuation of treatment if it was used for one year or less and occurred in ≥ 10% of the patients; each indication for drugs with multiple indications was assessed individually.
- The list of all approved drugs in Europe was downloaded from the European Medicines Agency (EMA) website from 1st January 2010 until 25th December 2020 [6]
- Only branded medicinal products were considered: generics, biosimilars and branded products with generic or biosimilar alternatives were excluded.
- Other exclusion criteria were: Metastatic cancer or locally/regionally advanced cancers; Adjuvant/neoadjuvant treatments; Treatments for chronic conditions; Paediatric treatments; Vaccines and prophylactic treatments; Surgical, diagnostic and medical devices
- The list of authorised drugs was assessed by 2 assessors to define a shortlist of drugs considered curative
- Each product Summary of Product Characteristics (SmPC) was reviewed to extract all of the licensed indications for each drug. Only indications that comply with the definition of cure were considered; when applicable, different subgroup of patients were also considered if the posology or treatment duration differed.
- Listed Drug prices were extracted from the public reference sources for prices in France and ex-factory prices were included.
- The cure rates for each drug were extracted from the pivotal clinical studies for each indication on a clinical endpoint relevant for that condition, reported in the SmPC or the European public assessment report (EPAR).
- The average treatment cost per patient for each indication was calculated based on the standard treatment plans described in the SmPCs in terms of dose, posology and length of therapy for each indication. Cost of treatment for drugs that are used in combination with other drugs as recognised curative treatment regimens were also considered, but no other healthcare resource utilisation was accounted for in this analysis.
- The cost per cure outcome was derived using the total treatment cost and cure rate, and categorised by therapeutic area.

Results

The list of drugs downloaded from the EMA website included 1,502 approved medicines for human use. Triage of those that are generics or biosimilars resulted in a list of 1,179 drugs, and on applying the additional inclusion and exclusion criteria, 33 drugs were identified as cures, of which 24 were reimbursed in France and for which prices were available by 31st March 2021. The summary of the drugs included in this study is in the table 1.

Table 1: Drugs included in the study, with the clinical study endpoints

Generic name	Indication	Cure endpoint
brentuximab vedotin	Lymphoma, Hodgkin previously untreated; Lymphoma, Systemic anaplastic large cell	CR
blinatumomab	Precursor Cell Lymphoblastic Leukemia-Lymphoma	CR
bosutinib	Leukemia, Myeloid	CR
isavuconazole	Aspergillosis; Mucomycosis	CR
decitabine	Leukemia, Myeloid	CR
delamanid	Tuberculosis, Multidrug-Resistant	CR(SCC)
fidaxomicin	Clostridium Infections	CR(GCR)
sofosbuvir / velpatasvir	Chronic Hepatitis C	SVR12
piperaquine tetraphosphate / artenimol	Malaria	CR(PCR)
Obinutuzumab	Leukemia, Lymphocytic, Chronic, B-Cell	CR
ledispavir / sofosbuvir	Chronic Hepatitis C	SVR12
glecaprevir / pibrentasvir	Chronic Hepatitis C	SVR12
gemtuzumab ozogamicin	Leukemia, Myeloid, Acute	CR
midostaurin	Leukemia, Myeloid, Acute	CR
bedaquiline	Tuberculosis, Multidrug-Resistant	CR(SCC)
tedizolid phosphate	Soft Tissue Infections	CR(M)
sofosbuvir	Chronic Hepatitis C	SVR12
meropenem / vaborbactam	Bacteremia; Bacterial infections (Respiratory Tract I; Pneumonia; Urinary Tract ; Intra-abdominal)	CR(M)
venetoclax	Leukemia, Lymphocytic, Chronic, B-Cell	CR+CRi
sofosbuvir / velpatasvir / voxilaprevi	Chronic Hepatitis C	SVR12
daunorubicin / cytarabine	Leukemia, Myeloid, Acute	CR+CRi
axicabtagene ciloleucel	Lymphoma, Follicular; Lymphoma, Large B-Cell, Diffuse	CR
ceftazidime / avibactam	Bacterial infections (Soft Tissue; Gram-Negative; Pneumonia; Urinary Tract Infections	CR(M)
elbasvir / grazoprevir	Chronic Hepatitis C	SVR12

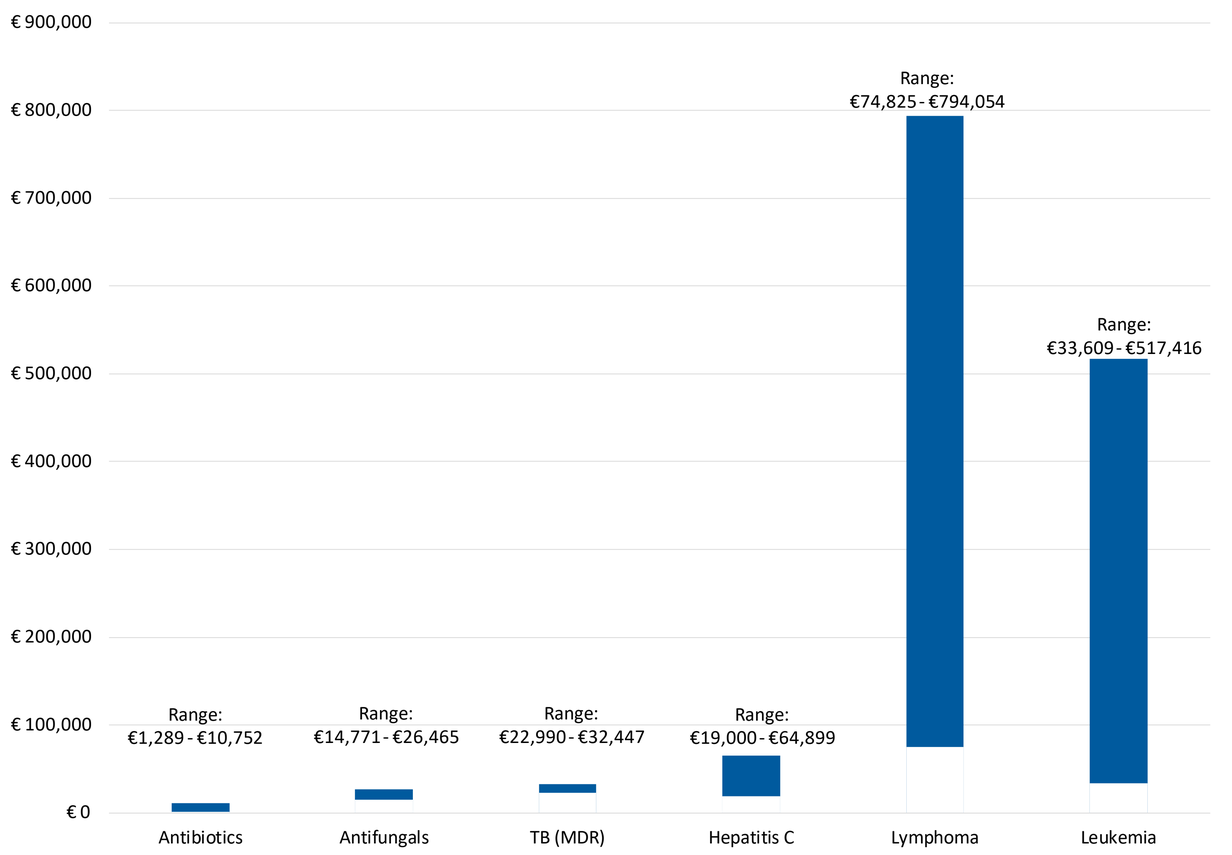
CR	*Complete response/complete remission*	*CR+CRi*	*Complete response & incomplete response*
CR(GCR)	*Global cure rate (Clostridium difficile)*	*CR(M)*	*Microbiological response*
CR(PCR)	*Complete response - corrected cure rate malaria*	*CR(SCC)*	*Sputum culture conversion (tuberculosis)*
SVR12	*Sustained virologic response at 12 weeks (hepatitis C)*		

The cure rates were highest for hepatitis C treatments (over 85% SVR at 12 weeks) for multiple indications relating to the different genotypes and presence or absence of cirrhosis. The average cost per cure for all the indications included in the study was €51,494 (range: €31 - €794k). The cost per cure for the haematological cancers had a very broad range (€34k - €794k) and was substantially higher than the cost per cure for all other conditions. This was particularly high for CAR-T cells, with an average cost per cure of €615,782. The average cost per cure for the oncology treatments, anti-infectives (antibiotics, antifungals) and hepatitis C treatments was €276,843, €8,023 and €31,418, respectively. The average cost per cure for antibiotics, excluding treatments for multi-drug resistant tuberculosis, was €5,504 (range: €1,289 - €10,752), which means that on average, to achieve a cure with an antibiotic, payers in France pay €5,504. The cost per cure for multi-drug resistant tuberculosis treatments ranged from €22,900 to €32,447. The anti-infectives had the lowest cost per cure across all therapeutic areas analysed, and within these, antibacterials had the lowest cost/cure in France. Budget impact and patient numbers are important factors to consider when discussing pricing, so an analysis stratifying by Orphan designation was done as a proxy for potential budget impact. The average cost per cure for the 11 orphan drugs included in the study, of which some have more than one indication, was €233k.

The average duration of treatment for the drugs included in this study was analysed. With the exception of the CAR-T treatments, oncology drugs had an average duration of treatment of 7.8 months/cycles compared to an average of 12 weeks for hepatitis C treatments. The longest duration of treatment for the other anti-infectives was 84 days for mucormycosis, with a median duration of 10 days. The summary of the drugs included in the study are listed in Table 1 which includes the endpoints from the clinical studies for the drugs. The cost per cure ranges are shown in Figure 1.

Results (cont.)

Figure 1: Average cost per cure across different therapeutic areas, in France



TB (MDR): Tuberculosis, multi-drug resistant

Lymphoma includes: Hodgkin lymphoma (previously untreated), systemic anaplastic large cell lymphoma (treatment-naïve), Chronic lymphocytic B-Cell Lymphoma, Follicular lymphoma, Large B-Cell, diffuse lymphoma.

Leukemia includes: Precursor cell lymphoblastic leukemia, myeloid leukemia, acute myeloid leukemia, chronic lymphocytic leukemia.

Discussion

This study sought to establish what the cost per cure for different therapeutic areas in France is. A significant variability across therapeutic areas was observed. The cost per cure for antibacterials was considerably lower than that of oncology treatments (the highest). This variance can be explained either by longer treatment durations and in some situations, by the higher prices of the drugs, or by the relatively lower clinical cure rates, reflecting the different characteristics of the diseases in the oncology setting.

Historically, antibiotics have been priced much lower than treatments for heart disease or cancer, with many antibiotics being off patent and therefore having a low price. Many payers have come to expect that all new antibiotics will be priced similarly, even the innovative antibiotics that target multi-drug resistant pathogens [7]. The negative impact of this pricing expectation is that several pharmaceutical companies have reduced antibiotic R&D [8, 9].

Generally, within reimbursement applications, antibiotics are assessed in the same way as other treatments and are expected to demonstrate that they provide better clinical outcomes than their existing comparator antibiotics [17]. However, microbiological data play a significant role in value demonstration, which is traditionally not recognised by payers as relevant information. Also, to protect their clinical effectiveness and minimise resistance, the new antibiotics are only used as a last resource, in a very small segment of the population, but without the incentives Orphan drugs have. Furthermore, clinical trials must have a non-inferiority design and are not in the population where these reserve antibiotics are expected to be used, which has implications for value demonstration for payers. Additionally, because antimicrobial resistance is a public health problem, the value to the general public in reducing the antimicrobial resistance could also be considered in reimbursement assessments[17].

The cost per cure is a simple but informative analysis for curative therapies, showing significant differences across therapeutic areas, however it has several limitations, such as:

- The use of list prices can significantly overestimate the costs for the healthcare system, introducing a significant limitation to the interpretation of the results of this analysis. During reimbursement discussions, confidential prices can, in many cases, be negotiated, where other factors are also considered, such as budget impact or country public health priorities. However, since these are confidential, any assumption made to estimate these could have introduce further bias to the analysis. Using the list prices was the most equitable option and the one is recommended to be used in gold standard cost-effectiveness analyses.
- The overall patient size, was not accounted for directly in the current analysis. Budget impact and affordability are one of the most important factors analysed by payers when considering the introduction of a new drug; this may impact the drugs' price, with treatments for smaller populations having the potential for higher drug costs, given the limited budget impact; this is frequently observed for Orphan drugs. In this study, drugs that had orphan designation, for rare conditions, with small patient populations, had substantially higher average cost per cure compared to non-orphans, with far larger patient populations, of €233k and €31k, respectively. This reflects the different existing incentives (financial or of other nature) for bringing to the market innovative drugs for rare debilitating conditions with high unmet need, where the patient numbers are small, and the drugs are therefore rarely used
- In this analysis, different endpoints and time points were used to define cure, depending on the therapeutic area. This is observed also in other health economic analyses, such as cost-effectiveness, where all the different clinical endpoints from the different therapeutic areas are converted in a model to Quality Adjusted Life Years (QALYs) enabling comparison of products across therapeutic areas. The cost per cure is in a way a simplified version of this analysis for curative therapies, where cure rates group a variety of clinical endpoints, with possible different baseline risk of relapse, which is not accounted for in this analysis.
- Patient populations are different across therapeutic areas. Even though only drugs approved for adult patients were included, the mean age of the patients affected by the condition, and its impact on health related quality of life, progression and severity, and unmet medical need may differ between different therapeutic areas.
- Only medicines approved by EMA were included. Medicines approved via mutual recognition procedure as well as de-centralised and national procedures were not included.
- The cost per cure was based solely on the drug costs, and excluded any healthcare resource utilisation costs, and the results should be considered in this context.

Conclusion

Despite the limitations of this research, it highlights the wide variation in the cost per cure across different therapeutic areas. Antibiotics offer a significantly better cost per cure ratio than other treatments that are generally far more expensive and do not provide a comparable cost per cure. With the increasing disinvestment in the R&D of antibiotics, it may be worth considering implementing new reimbursement incentives to encourage R&D into novel, targeted antimicrobial treatments.

References

1. World Health Organization, 2020. Antimicrobial Resistance. Accessed July 2021: LINK
2. World Health Organization, 2019. No Time to Wait: Securing the future from drug-resistant infections. Accessed January 2021: LINK
3. World Health Organization, 2017. WHO publishes list of bacteria for which new antibiotics are urgently needed. Accessed May 2021: LINK
4. World Health Organization, 2020. Lack of new antibiotics threatens global efforts to contain drug-resistant infections. Accessed May 2021: LINK
5. Albrecht B, et al., Pursuing breakthrough in cancer drug development. Here's how to get the right medicines to the right patients faster, in McKinsey Cancer Center. 2018.
6. European Medicines Agency. (2020). Accessed January 2021: LINK
7. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015, 40; 4: 277-283.
8. Hu C. Pharmaceutical companies are backing away from a growing threat that could kill 10 million people a year by 2050. Accessed May 2021: LINK
9. Baars C, & Lambrecht O. Pharmaceutical companies pulling out of antibiotic research. 2019. Accessed May 2021: LINK
10. McKenna M. We Need Antibiotics. They're Not Profitable To Make. Who Pays? 2015. Accessed May 2021: LINK
11. Petrelli et al. The requirements for manufacturing highly active or sensitising drugs comparing Good Manufacturing Practices. Acta Biomed. 2019, 90; 2: 288-299.
12. Bell J. Sandoz earmarks $175M to upgrade tech at European hub for antibiotics manufacturing. 2020. Accessed May 2021: LINK
13. Outterson et al. Repairing the broken market for antibiotic innovation. Health Aff (Millwood). 2015, 34; 2: 277-285.

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Corresponding author: sara.lopes@Shionogi.eu