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Physicians' preferences for prescribing oral and intravenous anticancer drugs: A Discrete Choice Experiment

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ABSTRACT

Although efficacy and tolerability are classical criteria for treatment choice, patient adherence and tariff issues related to novel oral anticancer drugs may also influence therapeutic decisions. We estimated the relative influence of efficacy, tolerability, expected adherence and route of administration of a chemotherapy treatment on 203 French physicians' preferences who participated in a Discrete Choice Experiment (DCE), a quantitative method used to elicit preferences. From a questionnaire with six scenarii, respondents had to choose between two treatments which differed with respect to these four attributes. Scenarii were first presented in a curative setting then in a palliative setting. Efficacy, tolerability and expected adherence had two modalities (good versus moderate) and route of administration had three modalities (intravenous (€286–379/session), oral with the current tariff (€28/consultation), oral with a hypothetical tariff (€114)). Efficacy was the reference criterion in choosing a treatment whatever the therapeutic goal (β: 2.114, $p < 0.0001$ in curative setting versus β: 1.063, $p < 0.0001$ in palliative setting). The oral route of administration was important but only in a palliative setting (β: 0.612, $p = 0.035$, and β: 0.506, $p < 0.0001$ for the current and hypothetical tariff, respectively). Removing the efficacy attribute from logistic regression model, tolerability (β: 1.228, $p = 0.0001$) and expected adherence (β: 1.223, $p = 0.0001$) were influent in curative setting while the route of administration was still predominant in palliative setting (β: 0.431, $p < 0.0001$). Results suggest that economic considerations as well as therapeutic efficacy play a significant role in choosing a treatment. Preference for oral chemotherapy with a hypothetical tariff for a patient support programme should be considered for the development of therapeutic education and healthcare coordination, currently not taken into account in the tariff of oral chemotherapy.

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1. Introduction

The development of oral anticancer drugs has had a major impact on classical cancer treatment pattern. Although guidelines recommend that treatments be chosen on the basis of efficacy and tolerability criteria, other factors, including optimising adherence, monitoring adverse side-effects, setting stage-specific treatment goals, improvement of quality of life, selecting eligible patients for oral treatments and tariff issues may also influence the medical decision-making process.[1–7]

When taking oral anticancer drugs, patients can receive their treatment at home rather than at hospital and previous studies demonstrated that, assuming equivalent efficacy, oral chemotherapy will be preferred to intravenous chemotherapy by patients with cancer.[1,5] On the other hand, among clinicians, the prescription of oral chemotherapy is still controversial. Despite the increased number of oral treatments that have been developed, intravenous chemotherapy still seems to be considered as the gold standard by many clinicians. This may be explained in part by the current French reimbursement system. Hospitals performing intravenous chemotherapy are reimbursed by the National Health Insurance on the basis of inpatient and outpatient hospital sessions, whereas the prescription of oral chemotherapy is mainly reimbursed on the basis of specialist consultation fees. Moreover, education and healthcare coordination required for oral chemotherapy are additional resources currently not taken into account in reimbursement tariffs and this may influence the prescription of oral chemotherapy. Reimbursement for oral chemotherapy is also an issue in the United States where it is excluded from the hospital insurance provided by Medicare (Medicare Part A). Patients who wish to receive the reimbursement of oral chemotherapy must subscribe to the additional Medicare Part B.[8,9] In this context, a US study demonstrated that health care providers who received more reimbursement prescribed more costly chemotherapy regimens for metastatic cancers.[3] This highlights the influence of the economic constraint on treatment choice.

Paradoxically, few published studies have investigated physicians' preferences[6,10–12] and most of the Discrete Choice Experiments (DCE) are conducted from the patient's perspective. The objectives of this study were: (i) to determine the relative importance of factors influencing the prescription of chemotherapy, (ii) to analyse the influence of the therapeutic goal (curative or palliative) on physicians' preferences, (iii) to determine if a higher hospital tariff for oral chemotherapy would be taken into consideration in therapeutic decisions.

In this study, *chemotherapy* was used as a generic term to describe all anticancer drugs (i.e. cytotoxic chemotherapy and targeted therapies).

2. Material and methods

2.1. Study population

Participants were selected from an exhaustive national database (CEGEDIM) that lists all physicians in France. Data on physician's age, gender, place of practice and geographical origin are documented in this database. Only participants qualified in oncology were selected namely oncologists, haematologists and other specialists qualified in oncology (radio-oncologists). We included medical specialties for which the disease can be treated with oral and intravenous chemotherapy and for which we assumed that a preference could thus be expressed (gastroenterologists, pneumologists).

2.2. Recruitment of participants and data collection

The study was carried out between November 2010 and January 2011. A letter introducing the aim of the study and a participation agreement with a prepaid return envelope were mailed to all eligible physicians ($n = 3277$). One reminder by fax, e-mail or telephone and one by mail were sent when necessary. Participants were asked to complete an online questionnaire.

2.3. The Discrete Choice Experiment questionnaire

Originally applied in social and economic research, Discrete Choice Experiments have recently been applied to medical issues in order to determine respondents' preferences for different healthcare interventions. Hypothetical scenarii are presented to respondents who are asked to choose between two or more options. Options are defined by specific attributes such as route of administration or cost with different modalities (for example, injection or tablet for the route of administration). The relative importance given to the proposed attributes can thus be determined and the trade-off that respondents make between these attributes and modalities is quantified.

2.3.1. Selection of attributes and modalities

Attributes and modalities were selected from published literature and their relevance reviewed by experts.[13–15] All factors which may influence the therapeutic decision in oncology were identified from a non-systematic literature review and classified into three groups, namely those relating to patient characteristics, those relating to disease characteristics and those relating to treatment characteristics. The list was presented to clinicians through semi-directive interviews to validate the relevance of items selected, to ensure that important factors had not been overlooked. Finally, only attributes relating to treatment characteristics were included in the questionnaire in accordance with the methodological literature.[15] These were efficacy, tolerability, expected adherence, route and tariff of administration. The first three attributes (efficacy, tolerability and expected adherence) had two modalities (good versus moderate) whereas the route and tariff of administration had three modalities: (i) intravenous (€286–379 per session in private and public hospital, respectively), (ii) oral with the current tariff (€28 per consultation) and (iii) oral with a hypothetical higher tariff (€114). The hypothetical tariff was included in order to analyse the sensitivity of respondents to a higher tariff when prescribing oral chemotherapy. This tariff was based on consulting fees adjusted for the longer consultation time needed for prescribing oral chemotherapy (€31 instead of €28), one initial nursing

consultation dedicated to patient education (€40), coordination of care between hospital, pharmacy and general practitioner plus telephone monitoring (€26) and routine hospital laboratory monitoring (€17). Descriptions of modalities were also given in the questionnaire for efficacy (antitumor activity improving survival ('good') versus partial antitumor activity ('moderate')), for tolerability (limited side-effects and toxicity which do not require ('good') or require ('moderate') a change in the therapeutic protocol), and for expected adherence (good cognitive abilities, and constructive family and social group ('good') or impaired cognitive abilities, and dysfunctional family and social group ('moderate')).

2.3.2. *Construction of the DCE questionnaire*

The combination of these attributes and modalities resulted in 24 ($2^3 \times 3^1$) possible scenarii. Among these 24 possible scenarii, six optimal scenarii were selected using a fractional factorial design (SAS® OPTEX procedure). For each scenario proposed, participants were asked to choose between treatment A and treatment B (Fig. 1). The questionnaire was divided into two parts, one evaluating a curative setting and the other a palliative setting to analyse the influence of the therapeutic goal on preferences. Both parts proposed the same six scenarii.

To minimise presentation bias, attributes were presented in a random order for each participant. Before the study, the DCE questionnaire was tested by a panel of physicians to ensure comprehension and ease of use. Before completing the questionnaire, participants were explained the DCE methodology and provided with definitions of each attribute and modality tested. Once participants had chosen between the twelve scenarii, they were asked an open question on other important attributes influencing their therapeutic decision: '*Other than the attributes proposed in the DCE questionnaire (efficacy, tolerability, expected adherence, route and tariff of administration), is there another factor which could influence your therapeutic decision?*'.

2.4. *Statistical analyses*

The importance of each treatment attribute in physician preference was assessed using a conditional logistic regression model based on the following equation: $V = \beta_0 + \beta_1$ ADHERENCE + β_2 EFFICACY + β_3 ROUTE + β_4 TOLERABILITY + ε, where V is the utility of a given chemotherapy regimen, β_0 is a constant reflecting the physician's preferences for prescribing treatment A versus treatment B, and β_1, β_2, β_3, β_4 are the β coefficients indicating the relative importance of each attribute. The signs of the β coefficients indicate whether the attribute has a negative or positive effect on utility. The higher the value of the β coefficient value, the stronger is the respondent's preference for a given attribute.

To take into account potential dominance of the efficacy attribute on other attributes,[16] an exploratory secondary analysis was performed excluding the efficacy attribute in order to assess the relative importance of the other attributes without taking into account the effect of efficacy (Model 2). Potential differences in preferences between the three groups of physicians (oncologists, haematologists, other specialists qualified in oncology) were taken into account by interaction terms in the model. All analyses were performed using SAS® software (Version 9.2, North Carolina, United States of America).

3. Results

3.1. *Sample characteristics*

Overall, 280 physicians agreed to participate, of whom 207 completed the questionnaire (74%). Four questionnaires were excluded, one because it was incomplete and the three others because they were completed by physicians who did not prescribe chemotherapy. The analysis was thus restricted to the 203 respondents qualified to prescribe chemotherapy. These included 84 oncologists, 60 haematologists and 59 other specialists qualified in oncology. Respondents were not different from the eligible population with respect to their geographical origin ($p = 0.796$) and type of medical practice ($p = 0.174$). The mean age of respondents was 46.4 ± 9.5 years compared to 49.5 ± 9.8 for non-respondents; 65% of respondents were male and 35% were female (Table 1).

3.2. *Respondents' preferences*

3.2.1. *Relative importance of attributes and modalities*

The relative importance of attributes and modalities for curative and palliative settings is shown in Fig. 2. The efficacy attribute appeared to be the dominant criterion for choice, with few physicians choosing a treatment with moderate efficacy (1% in the curative setting and 11% in the palliative setting). Modalities with an oral route of administration were more often chosen by physicians in the palliative setting (37% for oral chemotherapy with the hypothetical higher tariff and 34% for oral chemotherapy with the current tariff versus 29% for intravenous chemotherapy).

3.2.2. *Statistical analyses of physicians' preferences*

The results of conditional regression models are summarised in Tables 2a and 2b. In Model 1, the efficacy attribute had a significant effect on physicians' preferences both in curative (good efficacy versus moderate efficacy: $\beta = 2.114$, $p < 0.0001$) and palliative settings (good efficacy versus moderate efficacy: $\beta = 1.063$, $p < 0.0001$) especially for oncologists and haematologists (Table 2a). The route of administration had also a significant influence in palliative setting with a preference for modalities with oral route of administration ($\beta = 0.612$, $p = 0.035$ for oral route with the current tariff (€28) and $\beta = 0.506$, $p < 0.0001$ for oral route with the hypothetical higher tariff (€114)). In the exploratory secondary analysis (Table 2b), we found that tolerability (good tolerability versus moderate tolerability: $\beta = 1.228$, $p < 0.0001$) and expected adherence (good expected adherence versus moderate expected adherence: $\beta = 1.223$, $p < 0.0001$) also influenced treatment choice in a curative setting, especially for oncologists and haematologists. In the palliative setting, the route of administration remained the most important criterion for choice, with a preference for the oral route of administration with a hypothetical higher tariff for a patient support programme ($\beta = 0.431$, $p < 0.0001$), especially for haematologists and specialists.

Curative setting

Taking into account the characteristics of each treatment, what treatment option would you choose to treat a solid tumour or haematological malignancies?

Choose A or B among these two options.

ATTRIBUTES	TREATMENT A	TREATMENT B
Route and tariff of administration	Intravenous route (€286 - 379 €/session)	Oral chemotherapy (€31/consultation) with additional tariff for patient follow-up (83 €/year/patient)
Efficacy	Good	Moderate
Expected adherence	Good	Moderate
Tolerability	Moderate	Good
Which treatment would you prescribe?	**A**	**B**
Tick the box A or B	☐	☐

Palliative setting

Taking into account the characteristics of each treatment, what treatment option would you choose to treat a solid tumour or haematological malignancies?

Choose A or B among these two options.

ATTRIBUTES	TREATMENT A	TREATMENT B
Route and tariff of administration	Intravenous route (€286 - 379 €/session)	Oral chemotherapy (€31/consultation) with additional tariff for patient follow-up (83 €/year/patient)
Efficacy	Good	Moderate
Expected adherence	Good	Moderate
Tolerability	Moderate	Good
Which treatment would you prescribe?	**A**	**B**
Tick the box A or B	☐	☐

Fig. 1 – Example of a scenario presented in the questionnaire.

3.3. *Other factors influencing physician's therapeutic decision*

Among the 203 physicians, 70 respondents (34 oncologists, 16 haematologists and 20 other specialists) answered the open-question about other factors influencing treatment choice. Respondents could give multiple answers and ninety items were identified. The most frequently cited items were classified into one of four dimensions relating to patient, disease, treatment and environment features (Fig. 3).

4. Discussion

The relative influence of efficacy, tolerability, expected adherence, route and tariff of administration on physicians' preferences when prescribing chemotherapy were evaluated using a Discrete Choice Experiment. This study allowed quantifying the impact of reimbursement issues on the prescription of oral chemotherapy for the first time.

As expected, efficacy was found to be the dominant attribute driving treatment choice whatever the therapeutic goal. This is consistent with treatment guidelines. In the curative setting, tolerability, adherence and, route and tariff of administration were not influent. The lack of influence of the tolerability criterion on physicians' preferences is quite surprising since therapeutic decisions are generally based on the first assessment of the risk-benefit ratio which includes treatment tolerability. The low impact of adherence on treatment decision may be reflected by the fact that at the early stage of treatment management, patients are generally more compliant with their treatment than at the advanced stage of disease where compliance may decrease partly due to complexity of therapeutic protocols and length of treatment. In the palliative setting, the influence of tolerability and expected adherence was not statistically significant despite a high value of beta coefficients. This was explained by the fact that for two of the twelve pairs of scenarii proposed in the questionnaire, all physicians have chosen the same therapeutic option. This consensus on treatment preferences led in a lack of variability in physicians' choices and thus to a deviation in the model construction. Finally, the lack of preference for the oral route of administration in the curative setting may reflect preconceptions. In spite of evidence demonstrating equivalent efficacy of oral and intravenous route, the intravenous route is frequently considered by physicians as the most effective way to administer anticancer

Table 1 – Characteristics of the study sample.

	Non-respondents (N = 3074)	Respondents (N = 203)	p-Value[a]	Total (N = 3277)
Age (years)			$p < 0.001$	
Mean (SD)	49.5 (9.8)	46.4 (9.5)		49.3 (9.8)
Class				
<40	410 (17.2%)	50 (28.1%)		460 (17.9%)
40–44	403 (16.9%)	32 (18.0%)		435 (17.0%)
45–49	404 (16.9%)	35 (19.7%)		439 (17.1%)
50–54	404 (16.9%)	22 (12.4%)		426 (16.6%)
55–59	323 (13.5%)	17 (9.6%)		340 (13.3%)
60–64	292 (12.2%)	20 (11.2%)		312 (12.2%)
>65	151 (6.3%)	2 (1.1%)		153 (6.0%)
Missing data	687	25		712
Gender n (%)			$p = 0.028$	
Male	1757 (57.2%)	132 (65.0%)		1889 (57.6%)
Female	1317 (42.8%)	71 (35.0%)		1388 (42.4%)
Medical specialty n (%)			$p < 0.001$	
Oncologists	820 (26.7%)	84 (41.4%)		904 (27.6%)
Haematologists	1040 (33.8%)	60 (29.6%)		1100 (33.6%)
Other specialists qualified in oncology[b]	1214 (39.5%)	59 (29.1%)		1273 (38.8%)
Geographical origin[c] n (%)			$p = 0.796$	
Low medical density	334 (10.9%)	19 (9.4%)		353 (10.8%)
Moderate medical density	198 (6.4%)	13 (6.4%)		211 (6.4%)
High medical density	2542 (82.7%)	171 (84.2%)		2713 (82.8%)
Type of medical practice n (%)			$p = 0.174$	
Public hospital	2051 (66.7%)	128 (63.7%)		2179 (66.5%)
Anticancer centre	421 (13.7%)	39 (19.4%)		460 (14.0%)
Private hospitals	296 (9.6%)	22 (10.9%)		318 (9.7%)
Outpatient sector	144 (4.7%)	7 (3.5%)		151 (4.6%)
Other	162 (5.3%)	5 (2.5%)		167 (5.1%)

[a] ANOVA, Kruskal Wallis, Chi-2 and Fisher exact tests were used to analyse the representativeness of respondents versus non-respondents.
[b] Radio-oncologists, pneumologists, gastroenterologists.
[c] Regions were classified according to the density of physicians: low (68–104 physicians for 100,000 inhabitants), moderate (105–171 physicians for 100,000 inhabitants), high (172–527 physicians for 100,000 inhabitants).

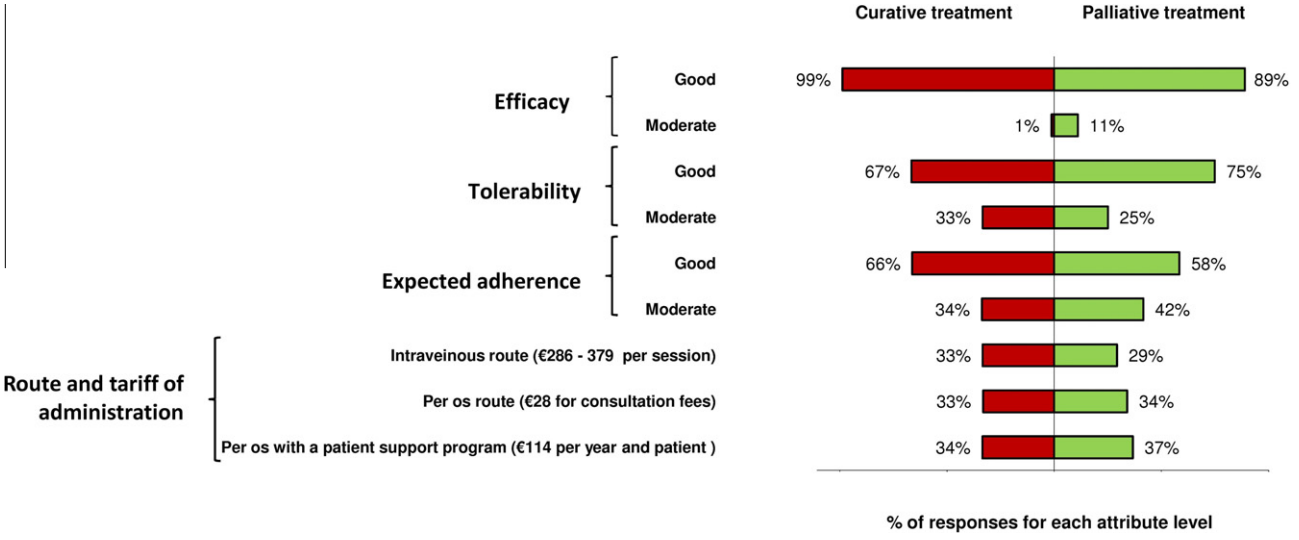

Fig. 2 – Description of the relative importance of treatment attributes and modalities.

drugs.[1] This may be explained by perceived difficulties with controlling adherence and managing adverse events, variations in bioavailability between patients, and hepatotoxicity associated with the use of oral chemotherapy.[17] These factors may affect the safe use and effectiveness of oral chemotherapy protocols and highlight the need for data on

Table 2a – Conditional logistic regression models of physician preference in curative and palliative settings (Model 1).

Attributes and modalities	All physicians (n = 203)		Oncologists (n = 84)		Haematologists (n = 60)		Specialists (n = 59)	
	β Coeff.	p-Value	β Coeff.	p-Value	β Coeff.	p-value	β Coeff.	p-Value
Curative setting								
Efficacy								
Good vs. Moderate	**2.114**	**<0.0001**	**2.411**	**<0.0001**	**1.701**	**<0.0001**	9.099	N.S
Tolerability								
Good vs. Moderate	0.227	N.S	0.159	N.S	0.203	N.S	4.567	N.S
Expected adherence								
Good vs. Moderate	0.139	N.S	3.36E-15	N.S	0.203	N.S	2.065	N.S
Route and tariff of administration								
Oral (€28/consultation) vs. Intravenous (€286-379 /session)	−0.204	N.S	−0.212	N.S	−0.271	N.S	0	–
Oral (€114/year/patient) vs. Intravenous (€286-379 /session)	0.146	N.S	−0.424	N.S	0.271	N.S	9.134	N.S
Palliative setting								
Efficacy								
Good vs. Moderate	**1.063**	**<0.0001**	**1.165**	**<0.0001**	**0.920**	**<0.0001**	2.992	N.S
Tolerability								
Good vs. Moderate	4.560	N.S	4.543	N.S	4.663	N.S	6.542	N.S
Expected adherence								
Good vs. Moderate	3.976	N.S	3.956	N.S	4.014	N.S	4.115	N.S
Route and tariff of administration								
Oral (€28/consultation) vs. Intravenous (€286-379/session)	**0.612**	**0.035**	−0.209	N.S	0.940	N.S	8.460	N.S
Oral (€114/year/patient) vs. Intravenous (€286-379/session)	**0.506**	**<0.0001**	0.355	N.S	**0.743**	**0.0003**	**0.461**	**0.037**

N.S Not significant
N.A Not applicable

Table 2b – Conditional logistic regression models of physician preference in curative and palliative setting (Model 2).

Attributes and modalities	All physicians (n = 203)		Oncologists (n = 84)		Haematologists (n = 60)		Specialists (n = 59)	
	β coeff.	p-Value	β coeff.	p-Value	β coeff.	p-Value	β coeff.	p-Value
Curative setting								
Tolerability								
Good vs. Moderate	**1.228**	**<0.0001**	**1.282**	**<0.0001**	**1.021**	**<0.0001**	4.555	N.S
Expected adherence								
Good vs. Moderate	**1.223**	**<0.0001**	**1.277**	**<0.0001**	**1.021**	**<0.0001**	4.547	N.S
Route and tariff of administration								
Oral (€28/consultation) vs. Intravenous (€286-379 /session)	−0.019	N.S	−0.0005	N.S	−0.059	N.S	2.17E-16	N.S
Oral (€114/year/patient) vs. Intravenous (€286-379 /session)	0.019	N.S	−0.023	N.S	0.059	N.S	0.034	N.S
Palliative setting								
Tolerability								
Good vs. Moderate	4.691	N.S	4.670	N.S	4.764	N.S	4.663	N.S
Expected adherence								
Good vs. Moderate	4.432	N.S	4.447	N.S	4.401	N.S	4.444	N.S
Route and tariff of administration								
Oral (€28/consultation) vs. Intravenous (€286-379/session)	0.095	N.S	−0.025	N.S	0.190	N.S	0.178	N.S
Oral (€114/year/patient) vs. Intravenous (€286-379/session)	**0.431**	**<0.0001**	0.263	N.S	**0.783**	**0.0002**	0.359	N.S

N.S Not significant
N.A Not applicable

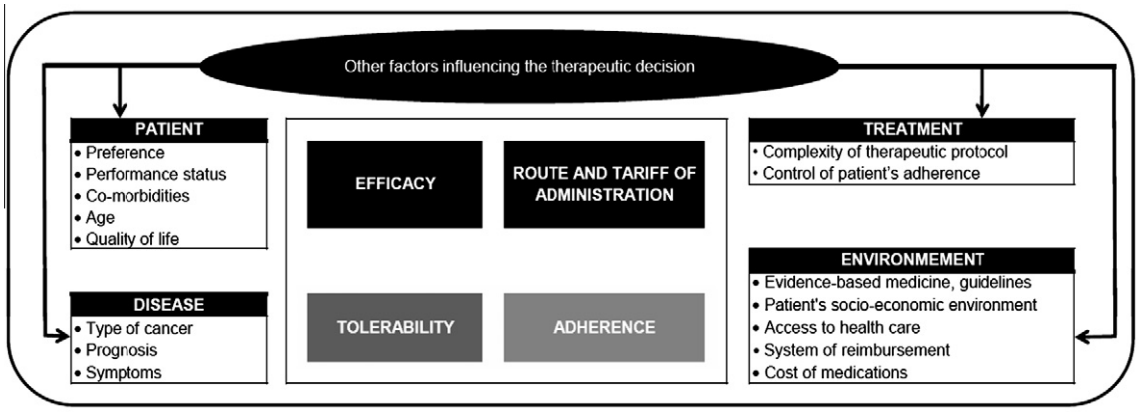

Fig. 3 – Conceptual model of medical decision-making in oncology: results of the Discrete Choice Experiment including responses to the open-question.

the effectiveness of oral chemotherapy under conditions of real-world use, which is currently poorly documented. In contrast, in the palliative setting, preference for the oral route of administration was observed, with respondents sensible to the tariff of a patient support programme. This highlights the sensitivity of healthcare providers to the issue of reimbursement that has been reported previously.[2,3] In contrast, the reimbursement issue does not appear to influence choice in the curative setting where the economic constraint is nonetheless also important.

Without taking into account the efficacy attribute in the secondary exploratory analyses, tolerability was a key criterion in a curative setting but not in a palliative setting, where patient quality of life is especially important.[7] As expected, we found that patient's adherence, in the curative setting, and reimbursement issues, in the palliative setting, may influence therapeutic decision.

DCE is a powerful multi-dimensional tool that can be used to analyse simultaneously the importance of multiple factors on medical decision-making, which would not be possible using unidimensional measures such as Likert scales. Despite the relative simplicity of the scenarii proposed in our questionnaire, each attribute and modality had a significant effect on preference (Model 1 and 2). They were also consistent with treatment guidelines. The DCE is also an appropriate method to test hypothetical scenarii which could be used to assess willingness-to-pay.

Several limitations of the study should be noted. In particular, the limited number of attributes and scenarii tested do not reflect the full complexity of medical decision-making in oncology. Indeed, chemotherapeutic protocols may include both oral and intravenous chemotherapy. A more detailed description of modalities for the attributes would have conducted to a better variability in treatment preferences. However, analyses were conducted on all chemotherapeutic treatments and not on a specific treatment. Thus the study objective was not adapted to a detailed description of modalities given in the questionnaire. This issue underlines a classical limit of the Discrete Choice Experiment (DCE) for which a limited number of attributes and modalities is required in terms of feasibility. Long and complex questionnaire leads to cognitive limitations and missing data. In this respect, the results of the open question allowed us to complete the DCE identifying other factors such as patient's preference, complexity of therapeutic protocols, and type of cancer which also influence treatment choice. Secondly, the preponderance of the efficacy attribute could be interpreted as a limit of the DCE when a 'hierarchical preference' is expressed by respondents, who always chose the treatment with the best efficacy regardless of other attributes.[16] Thirdly, the sensitivity of physicians to the hypothetical tariff for oral chemotherapy was not tested at different thresholds. Finally, the representativeness of the study sample was partial. The choice of variables was motivated by the use of classical variables (i.e. age, gender...), the availability of data on the CEGEDIM database and by assumptions on the influence of certain variables such as geographical origin, medical specialty and type of medical practice on therapeutic choice. Respondents were not different from non-respondents with respect to their geographical origin and type of medical practice but they were different with respect to age, gender and medical specialty. The distribution of the study sample by age was quite similar to that described in the National Council of the College of Physicians (CNOM) report (2011) presenting the physicians demographic characteristics. The way of administering the questionnaire over a web-based interface may contribute to the younger age of respondents compared to non-respondents. We achieved a higher participation rate in men (65%) than in women (35%). This figure seems to be consistent with data reported on the repartition of men and women among medical activities since the proportion of men involved in oncological specialties is higher than that of women (55% versus 45%, respectively). Finally, since cancer management is mainly the responsibility of oncologists, this speciality may have been more likely to participate and may contribute to explain the higher participation rate of oncologists.

In conclusion, our results suggest that tariff considerations as well as therapeutic efficacy play a determinant role when a choice is possible between oral and intravenous chemotherapy. Differences between curative and palliative settings highlight the importance of the therapeutic goal on treatment choice. In the palliative setting, the oral route of administration was preferred by physicians who were receptive to the imaginary scenario of oral chemotherapy with a

hypothetical higher tariff. This point should be taken into account when developing programmes for the safe use of oral chemotherapy involving patient education and healthcare coordination, and which need to be taken into account in hospital tariffs.

Ethics

The study design was approved by the CNIL (Commission Nationale de l'Informatique et des Libertés) under the declaration No. 1441480.

Conflict of interest statement

Laure Benjamin is a doctoral fellow whose researches are financed by GlaxoSmithKline (GSK) and the ANRT (Association Nationale pour la Recherche et la Technologie). François-Emery Cotté is employee of GSK. Qualees and Stat Process are Contract Research Organizations (CROs). Thomas Bachelot declares participating in a board of experts for GlaxoSmithKline (GSK). Gwenaëlle Vidal-Trécan declares no conflicting interest.

Role of the funding source

Funding for the study was provided by GSK and had no influence on the study design, execution and publication of results.

Authors' contributions

Laure Benjamin was responsible for the study design, monitoring, some statistical analyses, statistical interpretation and manuscript writing. François-Emery Cotté helped in the study design, statistical interpretation and manuscript preparation and review. Caroline Philippe was responsible for the recruitment of participants and data collection. Florence Mercier designed the DCE questionnaire and performed the statistical analyses. Thomas Bachelot helped in the questionnaire design and was responsible for questionnaire approval and manuscript review. Gwenaëlle Vidal-Trécan contributed to the study design, recruitment, manuscript preparation and submission. All authors reviewed and approved the manuscript.

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