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TITLE PAGE

Full-length title: Influence of conflicts of interest on public positions in the COVID-19 era, the case of Gilead Sciences

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Abstract

Fundings and gifts from the pharmaceutical industry have an influence on the decisions made by physicians and medical experts. In the context of the COVID-19 epidemic, several treatments are available to treat patients infected with the virus. Some are protected by patents, such as remdesivir, others are not, such as hydroxychloroquine. We wanted to observe the possible correlation between the fact, for an academic doctor in infectious diseases, of having benefited from funding by Gilead Sciences, producer of remdesivir, and the public positions taken by this doctor towards hydroxychloroquine. Our results show a correlation (correlation coefficient = 1) between the amount received from the Gilead Sciences company and public opposition to the use of hydroxychloroquine in France. This should open up the debate on the role of the interest links of doctors with pharmaceutical companies in the medical and scientific public debate.

Introduction

The influence of private interests on scientific research is a well studied research object (Lexchin 1993) (Dana, 2003) (Blumenthal, 2004). If the payment of substantial sums is recognized as a source of conflicts of interest, small gifts or meals offered are more tolerated. However, it has been shown that they influence the behavior of those who receive them (Katz, 2003). “There’s no such thing as a free lunch” claimed Nobel Prized Milton Friedman (Friedman, 1975). For example, it has been shown that intense contact with pharmaceutical companies is significantly associated with the prescription of recent drugs (Watkins, 2003), or more expensive drugs when an alternative exists (Sharma, 2018). The low value of these gifts does not take away from their influence: doctors who are offered meals by the pharmaceutical industry prescribe more promoted drugs (Dejong, 2016). The influence of these gifts is not well perceived by doctors, who consider it less influential than what their patients estimate (Gibbons, 1998). Doctors are aware that gifts from industry can influence their colleagues, but few recognize that they can influence them themselves (Steinman, 2001).

In France, since Law No. 2011-2012 of December 29, 2011 (1), companies producing or marketing pharmaceutical products are required to make public all the agreements they conclude, in particular with healthcare professionals, as well as the benefits (including meals and the costs paid for attending conferences) and the remuneration they grant them. It is the laboratories which are obliged to declare these payments which show a link of interest. A public site whose consultation is open to the public lists all these declarations: transparence-sante.gouv.fr. Since the start of the Coronavirus epidemics, the public authorities had to push or limit the use of candidate treatments for COVID-19. These decisions have become the subject of public debates, in the written, digital, television and radio press. To inform the debates, infectious disease physicians were asked by the media to give their point of view on the use of the different treatments.

Candidate treatments for COVID-19 can be divided into two categories: those that are protected by a patent held by a pharmaceutical company, such as Remdesivir, Kaletra - before Abbvie abandonned its rights to the drug following negative studies on COVID19 (Cao, 2020). Others are generic:

hydroxychloroquine, azithromycin. 39 companies are currently manufacturing hydroxychloroquine (Million, 2020) The choice of the drug by the public authorities therefore translates into a significant gain or loss for the various laboratories which hold the rights to a candidate molecule.

The conflict between hydroxychloroquine and remdesivir, started by a publication listing both as treatment candidates (Wang, 2020), has grown considerably, with announcements and counter-announcements as well as contradictory articles (Gautret, 2020) (Gautret, 2020) (Chen, 2020) (Chen, 2020) (Huang , 2020) (Tang, 2020) (Mahevas, 2020) (Magagnoli, 2020), which had a significant influence on the share price of the company Gilead Sciences, listed on the NASDAQ (See for example the statement by Anthony Fauci (2) from April 29, 2020, synchronized with an article published in the Lancet at the same time (Wang, 2020)). It therefore seems relevant to us to focus on the links of interest between Gilead Sciences and various opinion leaders, infectious disease physicians in France that are now stakeholders of this health crisis.

This debate led us to wonder about the role of pharmaceutical companies in the current therapeutic debate. We particularly question the laboratories that hold rights to a candidate molecule, in particular Gilead Sciences with Remdesivir. Are the medical researchers who have spoken in recent weeks in the debate on the use of hydroxychloroquine in a position of a conflict of interest? This is the question we wanted to answer by studying the links of interest between Gilead Sciences, producer of Remdesivir, and the doctors who took a stand for or against hydroxychloroquine.

Materiel and methods

To establish the list of French academic infectious disease physicians, we used the list of members of CMIT (Council of Teachers in Infectious and Tropical Diseases). In the list we obtained, 98 medical researchers were identified. Public interventions were defined as a direct expression of opinion in a media, academic or not academic. Non-academic newspapers included national newspapers, regional newspapers, television channels, radio channels. For each member of the CMIT, we did a systematic search on Google News to identify press reports containing the word Hydroxychloroquine and quoting

this member of the CMIT. We carefully read their interventions and classified their positioning on a scale of 1 to 5, 1 meaning that they were very unfavorable to the use of hydroxychloroquine, 5 that they were very favorable to it. “Very favorable” was defined as “having expressed a call for generalization of the use of hydroxychloroquine, or reporting a successful use of the treatment in the physician’s facility”. “Favorable” was defined as “having recognized a positive effect of hydroxychloroquine, while waiting for confirmation of results for taking further position”. “Neutral” was defined as “expressing the need for more studies for making any comment of the efficiency of the treatment”. “Unfavorable” was defined as “while still waiting for more results, expressing negative comments about hydroxychloroquine”. “Very unfavourable” was defined as “expression of anger towards the mediatisation of hydroxychloroquine, or a strict opposition towards the generalization of the use of hydroxychloroquine”.

Using the eurofordocs.fr website which aggregates the data from the transparence-sante.gouv.fr website, we listed the links of interest with the Gilead Sciences laboratory of all CMIT members, as well as their links of interest with all companies subject to the declaration on the Transparency Health platform. We finally established the average of the sums received from Gilead Sciences for each of the categories of researchers established by their positioning with respect to hydroxychloroquine; similarly, we have averaged the amounts received by all reporting companies. We performed a Spearman correlation test to explore the relation between position towards hydroxychlorquine and funding received by Gilead Sciences.

Results

A total of € 678,527 was paid by the company Gilead Sciences, manufacturer of Remdesivir in 7 years, to doctors who are members of CMIT (Table 1). This represents an average of € 6,924 per doctor. All reporting companies combined, a total of € 4,603,098 was paid to CMIT physicians between 2013 and 2019 (Table 2). There is a strict correlation (Spearman test, p=0,017) between the position of doctors towards hydroxychloroquine and the average amount paid to them by the company

Gilead Sciences between 2013 and 2019. In all, only 13 doctors out of 98 CMIT members did not receive any benefit, remuneration or agreement from the Gilead Sciences company between 2013 and 2019. Among these 13 doctors, 7 were very favorable to the use of hydroxychloroquine, 1 favorable, 1 neutral and 4 have not taken a position. On the opposite, among the 13 doctors that received the most important funding from Gilead Sciences, 6 were very unfavorable to the use of hydroxychloroquine, 1 unfavorable, 3 neutral and 3 have not taken a position.

Discussion

In this short work, we wanted to observe the influence of conflicts of interest, in the time of COVID was confirmed. Not surprisingly, we have shown a correlation but we have been impressed by the level of correlation, which is perhaps one of the explanations for the violence of the debate that has taken place concerning the use of hydroxychloroquine. None of the studies involving Remdesivir (Wang, 2020) or Lopinavir/Ritonavir (Cao, 2020) could show any effectiveness of these drugs in the could show effectiveness in the prevention of mortality or the reduction, and reduction of the the viral load of COVID-19, whereas 4 studies have now shown significant differences on: clinical course, radiological course, mortality, viral load (Million, 2020) (Yu, 2020) (Huang, 2020) (Membrillo de Novales, 2020). In addition, the issue of conflict of interest goes beyond that of practitioners, and also undoubtedly affects publishers and conference organizers, who also have links of interest with the most dynamic pharmaceutical manufacturers. The COVID crisis will make it possible to re-analyze many things, including the issue of conflicts of interest, a problem which is absolutely not resolved in many countries of the world, including France. It does not concern only doctors, this matter also concerns publishers and organizers of medical events, who are subject to the same types of financial conflicts. It is interesting to notice that major measures have been taken in France to fight conflicts of interest in politics, including mandatory declarations of patrimony during the course of the mandates of representatives to a national authority (HATVP), such measures have not been taken in the medical field.

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Table 1: Links of interest with Gilead Sciences between 2013 and 2019 depending on the position towards hydroxychloroquine (HCQ)

Position towards HCQ	Number	Average (€)	Median (€)	Extreme – (€)	Extreme + (€)
Very favorable	8	52	0	0	417
Favorable	6	1524	1208	0	4773
Neutral	14	9729	2729	0	48006
Unfavorable	7	11085	10547	234	31731
Very Unfavorable	9	24048	26950	122	52812
Did not take position	54	4421	2143	0	36706
TOTAL	**98**	**6924**	**2188**	**0**	**52812**

Table 2: Links of interest with pharmaceutical companies between 2013 and 2019 depending on the position towards hydroxychloroquine (HCQ)

Position towards HCQ	Number	Average (€)	Median (€)	Extreme – (€)	Extreme + (€)
Very favorable	8	6649	1558	42	30875
Favorable	6	10913	9999	42	24840
Neutral	14	62858	26339	585	291755
Unfavorable	7	61519	57529	11842	100358
Very Unfavorable	9	157939	130250	7498	543673
Did not take position	54	32451	19766	0	241267
TOTAL	**98**	**46970**	**21978**	**0**	**543673**