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Research Article

A Qualitative Study of Medical Oncologists' Knowledge and Views of Biosimilars in the United States

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ABSTRACT

Background: As the cost of cancer care continues to rise, biosimilars provide an important cost-saving treatment option. Thus, understanding barriers to biosimilar uptake, including perceptions of biosimilars among oncologists, is critical. We interviewed medical oncologists to examine their knowledge, attitudes, and perceptions of biosimilars.

Methods: A snowball method was used to identify and recruit oncologists in 2019-2020. Following informed consent, a trained study interviewer conducted the semi-structured telephone interview covering the following topics: 1) knowledge of biosimilars; 2) views of the efficacy of biosimilars; and 3) perceptions of the future of biosimilars in oncology, including barriers to their use.

Results: Interviews were conducted with oncologists (n=8) from four academic cancer centers. Median years of experience treating cancer patients was 7.5 (range = 4.5 to 10 years) and median number of cancer patients treated with biosimilars each month was 1 (range = 0 to 60 patients). Knowledge of biosimilars varied, although oncologists tended to lack knowledge of how biosimilar efficacy is established and expressed concerns about the lack of long-term data to support efficacy. Although these oncologists believed that biosimilars will become widely used, they noted that the lack of both long-term efficacy data and biosimilar knowledge are barriers to adoption.

Conclusions: This study provides evidence for the need for biosimilar education for oncologists, particularly around biosimilar efficacy. Oncologists were cautiously optimistic that biosimilar use would lead to a reduction in healthcare costs. These findings will inform a national survey of oncologists' knowledge and views of biosimilars.

Keywords

Biosimilars, Medical education, Oncologists.

Introduction

Following FDA approval of the first biosimilar in 2015, interest in this new class of drugs has burgeoned [1,2]. Like its predecessor, the generic drug, a biosimilar produces clinical effects that are indistinguishable from its reference drug or biooriginator [3,4]. Unlike generic drugs, however, which are chemically synthesized to yield products of identical molecular structure, biosimilars are created via living cells, using a unique manufacturing process that can leave minor alterations in the inactive drug components [3,5]. Critically, while biosimilars are not chemically equivalent to their reference drugs, their efficacy, quality, and potency are considered to be clinically equivalent [3,4].

Given that biosimilars are produced at a comparatively lower manufacturing cost [6,7], their use has expanded in recent years. By 2020, 40 countries approved the use of 262 biosimilars, with oncology biosimilars accounting for nearly half of this number [2]. While the use of biosimilars in oncology has grown dramatically, there are a number of obstacles facing oncologists and other clinicians in the clinical adoption of biosimilars, including knowledge gaps [8-10] and apprehension about biosimilar safety and efficacy particularly in the context of extrapolated indications, interchangeability, and pharmacy-led substitution [8,10-13].

In this study, we aimed to examine knowledge and attitudes towards biosimilars among oncologists to grow our understanding of biosimilar use and barriers to their use in oncology, and to inform the development of a larger survey of oncologists.

Methods

All study procedures were reviewed and approved by the Northwestern University Institutional Review Board.

Eligibility Criteria and Recruitment

Oncologists were eligible if they currently treated cancer patients in the United States and were fluent in English. Eligible oncologists were recruited to complete individual, semi-structured telephone interviews during 2019-2020. A snowball method was used to identify and recruit participants. First, we sent an email inviting several oncologists from the Robert H. Lurie Cancer Center of Northwestern University to participate in the study. Next, we asked those who participated in the study to provide the names of additional oncologists practicing at Northwestern or other U.S. medical institutions who may be interested in participating. These individuals then received an email inviting them to participate in the study. Interested and eligible individuals were scheduled for a telephone interview.

Study Interview

Following verbal informed consent, a trained study interviewer (authors KK, DM or DP) conducted the telephone interview using a semi-structured interview guide. The guide covered the following topics: 1) knowledge of biosimilars; 2) views of the efficacy of biosimilars; and 3) perceptions of the future of biosimilars in oncology, including barriers to their use. The interviews were audio recorded. Audio-recordings were transcribed verbatim and information that could identify participants was removed.

Analysis

Interviewers entered detailed notes for each question into an Excel database. Four team members (KK, KH, SS, ML) reviewed the interview notes to create a list of preliminary themes for each topic (i.e., knowledge, efficacy, future of biosimilars). Next, the list of themes for each topic was refined to reduce redundant or non-relevant themes. Finally, the study team members reviewed the transcripts to confirm the list of themes was complete or further refine the list, as needed, and identify exemplar quotes for each theme.

Results

Sample characteristics

Interviews were conducted with oncologists (n=8) from four academic cancer centers located in the Midwest; two of the centers were National Cancer Institute-Designated Cancer Centers. The sample consisted of equal numbers of males (n=4) and females (n=4). Median years of experience treating cancer patients was 7.5 (range = 4.5 to 10 years) and median number of cancer patients treated with biosimilars each month was 1 (range = 0 to 60 patients).

Knowledge of Biosimilar Drugs

Knowledge of biosimilars varied greatly. For example, some oncologists had little knowledge of biosimilars (numbers in parenthesis represent the participant ID):
Well, I guess, I'm a little bit, you know, unclear about the definition of a biosimilar…I mean, I would imagine a biosimilar is something that has a similar efficacy, or similar structure, as generic type medicines. That's what I would define it as. If that's the definition, I use it every day, numerous times. If it's a synthetic – if it's something different, you know, I – I don't know if I do (use it). (011)

Another participant also incorrectly identified biosimilars as being the same as generic drugs: "I know that there's biologic differences, but I don't, in my mind, perceive it as different than a generic." (005) One oncologist noted a general lack of understanding of biosimilars among oncologists: "It's a unique field that we don't know a lot about in terms of understanding it." (003)
Other oncologists reported a growing familiarity with biosimilars. One participant reported becoming aware of and comfortable with biosimilars through literature and endorsements from medical organizations:
I think we're getting more and more acquainted and (there is) more and more data coming out, and more and more societies endorsing (biosimilars). I think the comfort level clearly is going up. I would say I was a bit hesitant two or three years ago. There was some hesitancy in the community, in general, and it's gradually getting lesser. (008)

Another oncologist described their proactive approach to growing their understanding of biosimilars through participation on the pharmacy and therapeutics (P&T) committee and speaking with

drug makers:
"We talk to the manufacturers, like contacts at pharmaceutical (companies) and other industry leaders, and ask about how they make monoclonal antibodies, and that's sort of eased my anxiety about using these drugs because we just had no idea. (It was) uncharted territory." (006)

Perceived Efficacy of Biosimilar Drugs

Oncologists expressed unfamiliarity with the process of determining efficacy for biosimilars: "I don't know the degree of rigor that goes into the approval and what levels of efficacy have to be met." (003) In particular, oncologists expressed concern about the lack of long-term efficacy data: "Part of the problem is that we don't have long-term data with all of this because it's all relatively recent." (004) another oncologist emphasized the importance of long-term data for cancer patients: "Short-term data for biosimilars is it either works or it doesn't. With oncology. There's not that much room for error. And the ramifications of being wrong are potentially life threatening." (011)

The importance of long-term efficacy in oncology was echoed by this oncologist:
I think that we have similar efficacy from the standpoint of initial responses, but I can't speak to what the long-term effects would be, especially when we're talking about these low-grade lymphomas where it really is something that evolves over a great deal of time to really see whether things (drugs) are just as effective or not… I think that it's different with the Neulasta biosimilar where the effect of it is almost immediate, whether you see something working or not because it's really meant to boost immune systems within the cycle of therapy. And so less reliant really on efficacy down the road. So, part of it is what kind of biosimilar are we dealing with? If it's something that we're going see immediate effects from and get relevant data for up front versus whether it's going to take a while to get that information, and that factors into whether we would adopt it. (004)

When asked if she had reservations about using biosimilars with her patients, participant 004 said, "Yeah, I do and I probably would say that I feel like some of our people in our practice would have similar reservations. I don't know what the breaking point is to say that we should use the biosimilar over Rituxan." Additionally, oncologists expressed concerns about the efficacy of biosimilars in the context of extrapolation, or the approved use of biosimilars in an indication studied and approved for the reference drug, but not studied in the biosimilar:
It (Rituximab) has been universally used across all B-cell lymphomas. Whereas the biosimilar is only purely approved for the low-grade lymphoma. And so, when we think about things being interchangeable, it's hard to say that that is indeed the case because it's (the biosimilar) really only been looked at in low grade (lymphoma), where we have data to say that Rituximab has improved survival across various different histologies for B-cell lymphoma. So, that concept of well, Rituxan I can use across the board, you don't have to really think much about it, that it's effective across the board. Can we really say that about the biosimilar? I'm not sure we can. (004)

Extrapolation, when oncologists were aware that it occurred, was unsettling, as noted by a thoracic oncologist who recalled that the clinical trials to support the biosimilar were conducted with samples of lung and colorectal cancer patients:
Interviewer: And how did you feel about that? The fact that it's a trial done in a different population or a mixed population?

Participant 007: I was certainly hesitant correlating from another kind of tumor type to lung cancer. I think there's a lot of potential unknowns there. Just when we look at different other agents between tumor types, there is not often an exact correlation and efficacy in what their response rates are, and so it's a little bit nerve racking.

Other oncologists also described discomfort with extrapolation:
I would be a little leery about it, frankly, because biosimilars as being, you know, that same, and I think subtle differences in molecular structure I think can make differences as it relates to cancer therapy, so I would feel hesitant about using a medicine of that capacity if there is an FDA approval and/or level 1 evidence indicating that another medicine is effective. (011)

But if there is really no data at all, and it's a complete kind of separation from another condition and there is really not much similarity between both other than in theory, I wouldn't consider it like standard of care, or I wouldn't offer it to everybody. (009)

However, as noted previously, concerns about efficacy may diminish with use, as noted by an oncologist whose practice had been using biosimilars for over a year:
I think initially I was hesitant. I was a little skeptical that (biosimilars) would work because hadn't had any experience with biosimilars. I mean, of course, we use generic medications, but we weren't sure if it would translate to the same level of efficacy. In addition, because the decisions made by my institution and the P&T committee related to cost issues, we really had no choice. We made a decision as a practice to use biosimilars…I think in terms of efficacy, I really don't see anecdotally a big difference and so – and I feel very comfortable using biosimilars. It makes a lot of sense from a practice perspective and some of that skepticism initially I think it was because of the unknown, but they seem to have same level of efficacy. (006)

Future of Biosimilars

Two themes emerged from the interviews regarding the future use of biosimilars: increased availability and reduced costs.

Increased availability

Most oncologists expected significant increases in the availability of biosimilars in the coming years, and one even noted that biosimilars will become "leaders in the market." However, patent laws were recognized as a barrier to greater availability of biosimilars:

There's a lot of regulatory issues that are preventing biosimilars being brought to the market. There's many that have been FDA approved, but they are not to the market yet. That's because of patent laws and things like that that are preventing free flow of the biosimilar. Right now, we don't have that many to choose from, although I do feel like in the next five years, or three years, there will be a lot more to choose from. (005)

Reduced costs

When discussing the future of biosimilars, nearly all oncologists discussed expectations that biosimilars would reduce the overall cost of oncology treatment in time. Reduced costs were expected because of increased competition in the market once current patent laws that are preventing biosimilars from coming to market are resolved:

I think (use of biosimilars) will be increased. I think that there will be changes in patent laws to make them easier to come to market. I think they will add competition where there is needed competition. And I think it will ultimately be one component of many that have the potential to lower the overall cost of chemotherapy or injectable drugs. (005)

Another participant emphasized the current cost burden in cancer care:

From an overall healthcare perspective, it's just astronomical what we're spending on care and it's a burden to society and to individual patients. I hear a lot about financial toxicity. Increasingly, patients are having trouble meeting their financial requirements and so I think it's a way to kind of – an adaptation of biosimilars is a way to kind of offset some of these cost issues and the burden (O06).

However, while one oncologist foresaw an overall reduction in cost of cancer treatment as a benefit, he expressed concerns that cutting costs too much could lead to lower standards for the manufacturing and development of biosimilars.

Barriers to the Use of Biosimilars

Oncologists acknowledged that inadequate knowledge of biosimilars and discomfort using them were barriers to their use. Participant 008 said, "I think the comfort level from both providers and patients…has gotten a lot better in the last two years, but I think it still has a way to go. I think you do sense that the comfort level is much more in academic institutions."

Other reported barriers to use of biosimilars were lack of long-term efficacy data: "We'd like to see more data because, of course, we want to deliver the best care possible to our patients and it's such a pivotal part of how we treat." (006) When asked what they thought were the biggest barriers to biosimilar use in oncology, one participant said, "Knowledge. Education. Efficacy. Perceived lack of evidence. But I think number one would be we just are unaware. We know they exist, but we're unaware of the data." (005) Participant 008 also emphasized the need for education, especially in small oncology practices:

I think that would be really a key push from the pharmaceutical company perspective is really getting into the physicians' offices with more information addressing those concerns of the physicians. I think that will be key over the next few years in terms of having more and more providers prescribing biosimilars and that becomes really key for the smaller practices where (the doctors) make the decisions (008).

This participant noted that for large academic institution, doctors are guided by institutional formularies. However, they noted in smaller practices, oncologist education will be the key to greater acceptance and use. Participant 004 echoed this sentiment, "Education is always certainly important. Having some exposure to some of this information repeatedly. Hearing about it more and more is always one of those things that helps."

Discussion

As the cost of cancer care continues to rise [14], biosimilars provide an important treatment option with the potential to lower treatment costs. Thus, understanding the barriers to their uptake is critical, particularly as patents expire for the most prescribed cancer reference drugs and their biosimilars enter the market [15,16]. Physician and patient perceptions of biosimilars are "likely to be the most complex of factors in the rate of adoption."[16] (p.1263) Current understanding of physicians' perceptions of biosimilars primarily comes from surveys of physicians in Europe10 and surveys of physicians across specialties (i.e., outside of oncology) [17]. Thus, there is a need to better understand views of biosimilars among oncologists in the United States.

Similar to other studies of cancer providers [18,19], we found considerable need and interest in education on biosimilars. Knowledge of biosimilars varied widely among the oncologists in our study, even with our small sample. Some oncologists did not understand what differentiated biosimilars from generics, for example. However, with growing exposure to biosimilars via literature, participation in P&T committees, input from industry representatives, or direct experience, oncologists reported becoming more comfortable with biosimilars. Thus, incorporating biosimilars into practice could be facilitated by educating oncologists about their manufacturing and approval processes first, as oncologists may be wary of the change to biosimilars. Our findings support observations by Nabhan and colleagues [16], who noted that oncologists may be most hesitant to accept biosimilars in the curative setting. Our findings also highlight the reluctance among oncologists to accept biosimilars without long-term efficacy data; thus, suggesting that education alone may not be sufficient to reduce reluctance among oncologists.

These results come from a small sample of oncologists in the Midwest region of the United States. These exploratory findings should be confirmed in larger samples of oncologists. To this end, we used these results to design a national survey of oncologists [20], to further assess knowledge of biosimilars, comfort with their use, and interest in further education about biosimilars.

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