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ORIGINAL ARTICLE

What constitutes meaningful benefit of cancer drugs in the context of LMICs? A mixed-methods study of oncologists' perceptions on endpoints, benefit, price, and value of cancer drugs

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Background: The importance of surrogate endpoints, magnitude of clinical benefit of cancer drugs, and their prices have often been debated in the oncology world. No study, however, has systemically explored oncologists' perception regarding these issues.

Methods: We conducted a mixed-methods study including in-depth qualitative interviews of medical oncologists prescribing cancer drug therapy in India. Quantitative data were collected using a predetermined proforma. Qualitative in-depth interviews were audio-recorded, transcribed verbatim, anonymized, subsequently coded, and analyzed by generating basic and global themes.

Results: We interviewed 25 medical oncologists. Twenty-eight percent of oncologists rarely used cancer drugs that improved response rate (RR) but not overall survival (OS), and an equal percentage mostly/often used such drugs. For cancer drugs that improved progression-free survival (PFS) but not OS, 20% never/rarely used them while 48% mostly/often used them. Oncologists in India considered a 4.5-month (range, 1.5-12 months) advantage in median PFS as meaningful, and considered price of ∼120 United States Dollars (USD) per month (range, 48-720 USD per month) for those PFS gains as justified. For OS, median gains of 4.5 months (range, 2-24 months) and at a monthly price of ∼360 USD (range, 48-900 USD) was considered justified. Oncologists in India were aware and concerned that RR only meant tumour shrinkage not survival benefit, but many assumed that tumour shrinkage meant better quality of life. Many oncologists acknowledged the limitations of PFS but would use a drug with PFS benefit if it was cheaper than the drug with OS benefit.

Conclusions: Oncologists in India showed awareness of the limited surrogacy between RR/PFS and OS but assumed that RR/PFS correlated with improved quality of life and acknowledged price as a factor in deciding treatment choices. This is the first study providing a benchmark for minimum clinical benefit (4.5 months in PFS or OS) and maximum monthly price (120 USD for PFS, 360 USD for OS) deemed justifiable by oncologists practicing in low-and-middle-income countries.

Key words: surrogate endpoints, PFS, clinical benefit, price, value

INTRODUCTION

The value offered by new cancer drugs, i.e. the clinical benefit they provide in relation to their prices, has been a matter of important clinical and policy discussions in recent years, both in high-income countries (HICs)[1-4] and low-and-middle-income countries (LMICs).[5-7] Cancer drugs have been criticized for their marginal gains,[8] high prices,[2,3,9,10] and uncertain clinical benefit because of approvals based on unvalidated surrogate endpoints.[11-14] Physicians' opinions regarding new cancer drug approvals based on surrogate endpoints, magnitude of clinical benefit, and pricing of cancer drugs seem to be diverse on media and social media, however, to our knowledge, this has not been systematically studied before. In addition, much of this discussion regarding what constitutes a high-value drug, and the justification of the pricing of these drugs, have been derived from research conducted in the settings of HICs.

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The burden of cancer is increasing in LMICs, however, with rising incidence and prevalence. LMICs share almost 70% of global cancer mortality.[15] Patients in LMICs lack access to new cancer drugs, however, mainly due to unaffordability and therefore, prioritization of cancer drugs is even more important in LMICs, given limited resources.[16] This double whammy of increasing cancer burden with rising drug prices can make cancer treatment unsustainable in LMICs, which need to urgently make prioritization decisions. International organizations such as the American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), and National Comprehensive Cancer Network (NCCN) have developed tools (ASCO value framework, ESMO-Magnitude of Clinical Benefit Scale, and NCCN blocks, respectively) to evaluate the magnitude of benefit from cancer drugs and make prioritization decisions. There is, however, very little input into these tools from the perspective of LMICs. Perception of LMIC oncologists working in resource-limited settings on the value of treatments is important to make prioritization decisions that are relevant to LMICs. Furthermore, it is also important to assess the awareness of LMIC oncologists regarding issues surrounding trial endpoints and prices of cancer drugs. It is not yet known whether and how LMIC oncologists (or even HIC oncologists, for that matter) consider issues related to endpoints, benefit, and price of cancer drugs in their daily clinical decision-makings.

Therefore, we conducted a mixed-methods study of oncologists from India to explore their perceptions regarding various endpoints used in cancer trials, magnitude of benefit, price of drugs, and how they made therapeutic decisions in their daily practice.

METHODS

The study received approval by the ethics committee (2020/TMC/174/IRB4) of Tata Medical Center, Kolkata. The study followed a cross-sectional mixed method design incorporating quantitative questions and qualitative in-depth interviews of medical oncologists. A methodological orientation of content analysis underpinned the conceptualisation of the study. The interview questions were developed by the authors, who have a rich experience of practicing oncology in low-resource settings, as well as experience with mixed-methods study. The study questions were initially piloted with five oncologists and revised based on that feedback. The objectives of this study were to explore the perceptions of cancer clinicians in India (i) about the benefits of cancer treatment based on three outcome measures: overall survival (OS) (clinical endpoint), response rate (RR) (surrogate endpoint), and progression-free survival (PFS) (surrogate endpoint); (ii) minimum magnitude of clinical benefit that would be considered acceptable in the local context; and (iii) the price for a cancer drug or other treatment that would be deemed justified for the given benefit in the Indian context. The study adhered to the COREQ guideline for reporting qualitative research.[17]

Research team

The research team consisted of a mix of oncologists who practiced in LMICs, a clinical psychologist, and two consultant psychiatrists working in the field of psycho-oncology and with extensive experience of qualitative research in an oncology setting in LMICs. None of the researchers were part of the oncology teams from where the respondents were selected. There were two women and four men in the research team reflecting the usual gender ratios in clinical and research teams in India.

Participants

Medical Oncology consultants in India prescribing drug therapy for patients with early and advanced cancer were invited to participate in the study. Only those clinicians with >2 years of experience in solid tumour oncology were included to ensure that our sample constituted oncologists with enough experience. Oncologists were invited for participation based on a hierarchical snowball method through an existing network of oncologist contacts in India. The potential participant was approached either face to face or by telephone, and this was followed by an email explaining the study rationale and a study information leaflet was shared with them. Participation was voluntary and respondents were included only after obtaining written informed consent from the participants. In-depth qualitative interviews were conducted by two researchers (SSD and AM) who were both trained in qualitative interviewing methods. To prevent any bias due to the fear of being judged by an oncologist colleague, all interviews were conducted by psycho-oncologists. Participants were given the option to discontinue participation after recruitment, if they so desired.

Interview procedures

Data collection was done by the researchers (SSD and AM) who are both consultant psychiatrists and experts in qualitative interviewing and data analysis methods. Interviews were conducted at a time that was convenient for the participant. Special care was taken to ensure adequate privacy during the interview and it was done over online video call from the work place of the clinician. There were no other persons present at the time of data collection, other than the interviewer and the respondent to ensure absolute privacy. Quantitative data were collected using a predetermined proforma. Qualitative data were collected through in-depth interviews. All interviews were audio-recorded, and verbatim transcripts were created for analysis. Transcriptions and data were stored securely at Tata Medical Centre, Kolkata. Each respondent was interviewed only once during data collection and transcripts were not shared with the respondents. Field notes were maintained by the researcher during each interview. Data collection and data analysis were done side by side to explore further details of the themes generated in subsequent interviews. Data collection was stopped after reaching data saturation in terms of similar content and themes being generated and no new information emerging with additional interviews.

Data analysis

Quantitative data were analyzed using simple descriptive statistics. Categorical data were described by percentage and proportions. For continuous data, median score with interquartile range (IQR) and overall range were used. For example, when the respondents were asked about the minimum gains in PFS and OS expected of new cancer drugs as well as the price for those gains that were deemed acceptable, the results describe the medians and ranges of their responses.

Qualitative analysis

Thematic analysis was followed during data analysis of qualitative data using the methods described by Braun and Clarke.[18] Qualitative in-depth interviews were transcribed verbatim by one of the researchers (VS) and cross-checked by another senior investigator (SSD). All transcripts were anonymized and subsequently coded manually by two independent researchers (SSD and VS) in the team using the principles of the thematic analysis. The codes were reviewed by a third senior researcher (BG) who sorted out any discrepancy between the two coders. Qualitative data were analyzed in the following steps: (i) thematic analysis was used to generate codes, (ii) data synthesis was carried out and basic themes were generated, (iii) global themes were generated by grouping the basic themes using the methods described by Braun and Clarke.[18]

RESULTS

A total of 30 oncologists were invited to participate, of whom 25 (age range, 31-54 years) had been practicing oncology for a median of 10 years (range, 4-20 years) and participated in this study (Table 1). Our cohort included 76% males, which is consistent with the demographics of oncologists in India.[19] Five oncologists did not participate as they were unable to provide a time for the interview due to their busy clinical schedule. The mean duration of the interviews was 35 min. In the verbatim quotes included in the results and tables, numbers after P indicate participant number (e.g. P10 means participant 10).

Perceptions regarding response rates

Only 28% of physicians indicated that they felt comfortable using a medication that improved only RR but not OS, with 44% indicating that they would occasionally use it and 28% rarely using it. Participants' concerns regarding the use of drugs based on RR alone could be summarized into the overlapping themes of concerns regarding survival benefit, quality of life (QoL) benefit, and toxicity profile (Table 2).

Among participants who felt comfortable with the RR endpoint, a consistent theme emerged, which is a presumed improvement in QoL with tumour shrinkage. In addition, a couple of oncologists considered downstaging of disease and tumour invading important structures as their considerations. The third theme was that of the patient's or family's request for continued treatment (Table 2).

Some oncologists expressed that they would accept RR as a good enough endpoint in some special situations, such as for generics or biosimilars or in rare cancers where alternatives are lacking (Table 2).

Perceptions regarding progression-free survival

The majority of the physicians (52%) indicated that they would never (4%), rarely (16%) or occasionally (32%) use a drug that improved PFS but not OS, with 36% indicating that they would often use it and 12% would always use it.

During the in-depth qualitative interview, cost featured more prominently while discussing PFS compared with

Table 1. Sociodemographic details of medical oncologists who participated in the study

Variables		Median (IQR), $n = 25$
Age, years		40 (IQR 36.5-42); range 31-54
Number of years since MBBS		15 (IQR 13-19.5); range 8-27
Number of years in oncology		10 (IQR 6.5-12.5); range 4-20
Reported percentage of time spent on diverse types of activities	Direct face-to-face clinical work	60 (IQR 50-75); range 25-85
	Non-direct clinical work (documentation, MDT, etc.)	10 (IQR 10-15); range 5-25
	Research/academics	15 (IQR 10-20); range 5-40
	Management	10 (IQR 5-17.5); range3-40
		Frequency (%) $n = 25$
Sex	Male	19 (76%)
	Female	6 (24%)
Organ based specializations[a], *n*	Breast	19
	GI tract	19
	Lung	17
	Sarcoma	17
	Head neck	16
	Gynaecological	15
	Urology	15
	Neuro-oncology	10
How often do you feel time-pressured about day-to-day clinical work due to work pressure?		Median 2 (IQR 1-3); range 0-3
How often do you feel stressed about day-to-day clinical work due to work pressure?		Median 2 (IQR 1-3); range 0-4

GI, gastrointestinal; IQR, interquartile range; MBBS, Bachelor of Medicine and Bachelor of Surgery; MDT, multidisciplinary team.
[a]Majority of the respondents managed patients from several organ/sites.

Table 2. Summary of qualitative themes and examples for response rates

Qualitative themes	Examples
Reasons against RR	
1. Effect on survival or quality of life	'Ideally response rate and survival should go hand in hand. If it is not, then there should be other factors that are causing it not to be reflected in the survival benefit' (P1) 'Response rate is more about the tumour. But I think in the treatment of cancer, it is not only the response of the tumour that is important.' (P23) 'just reduces the size, but does not improve the symptomatology, quality of life, or the time that the patient is alive. I highly doubt the benefit of the treatment.' (P25)
2. Toxicity	'the drug may have some toxicities because of which patients are not living longer' (P1)
Reasons in support of RR	
1. Symptom relief or improved QoL	'even if the overall survival does not improve compared to standard of care, I would use that regimen utilizing its response rate, because that will be for good palliation and symptom relief. But if symptom relief is not my concern, then I will not use something which has its impact only on the response rate and not on the overall survival.' (P9) 'patient in the stage IV disease the only intent of treatment is palliative. In that case, we don't offer any kind of treatment that will probably prolong life. The treatment is for improving the quality of life.' (P5) 'We can get symptomatic improvement by decreasing the tumour-size and we take response rate as an endpoint……If a patient shows a rapid response to chemotherapy, that leads to improvement in quality of life.' (P3) 'If the patient is very symptomatic from their disease, then symptom control is my first goal. That is when I will use it (response rate).' (P7) 'When the goal is to improve the overall quality of life, I will use response rate.' (P8) 'Response rate as defined by RECIST criteria translates into better PFS. Improved PFS translates to better quality of life. Medication may not be adding years to life but will be adding life to years. I use medication that increases the response rate as defined by RECIST criteria.' (P16)
2. Downstaging disease	'It helps in downstaging of the disease.' (P2) "At times the growth could be invading important structures that could be life-threatening, e.g. the airways. In this situation if you don't get a response, it is difficult to continue to treat the patient." (P13)
3. Something is better than nothing	'Most of the patient's family members think that giving something might improve things a little bit or that the patient can pull a few days longer or add on to their lives. If they insist on that and if the performance status of the patient is good and depending upon the cancer the patient has, I may use a medicine based on response rate.' (P18)
4. Impact of approval and guidelines	'In rectal cancer, I would take survival rate as an endpoint. In breast cancer, we are looking for a pathological complete response as an endpoint. Sadly, FDA has made this as an endpoint, and our chemotherapy or post-surgery treatment is guided by the pathological complete response rate. So, all the guidelines include it, and it is not possible not to discuss that. So, you are talking about response rate and not survival there, in early breast cancer, sadly.' (P6)
Case by case basis	
1. For cheaper generics or biosimilars	"Many Indian companies come with a generic, they get the approval based on the response rate. So, it's a phase II study. So, for phase II studies on bio-similars, the response rate is good enough as an endpoint. But, not in the routine clinical practice." (P1)
2. For rare cancers or lack of alternatives	"When I am treating uncommon cancers or a particular scenario where I don't have routine options available or I've exhausted the routine treatment options in a second- or third-line setting, I may accept a response rate as a good enough endpoint. But not in a first-line setting, not while treating very common cancers, or in situations where I have multiple options available." (P10)

FDA, Food and Drug Administration; PFS, progression-free survival; QoL, quality of life; RR, response rate.

during discussion of RR (Table 3). Participants expressed their preference to use drugs based on PFS assuming that they are cheaper than drugs that improved OS.

One participant described the pressure to adopt PFS due to PFS being adopted widely in medical literature, and another participant would use drugs with PFS benefit if it also improved QoL, but lamented the lack of studies done locally:

"I know I can't cure the disease, but providing a good progression-free survival along with an improved quality of life is something I'll be very happy to consider. I believe there are too many biases in these studies from the West and those from India. All of us are not willing to come together to study things and get rapid and quick answers." (P8)

Overall survival

When asked about their perception of OS as the trial endpoint and if there were situations where OS was not a good endpoint, participants expressed their comfort and satisfaction with using drugs that have demonstrated OS gains, especially when justifying the high prices of newer molecules. Some examples include:

'I would prefer to use a therapy because overall survival has shown a benefit.' (P1)

'If I am using a targeted agent or immunotherapy, it is a costly molecule. Then I will first look for the overall survival benefit.' (P2)

'Any intervention in oncology, be it curative or be it in a palliative setting, if there is an OS benefit, we take that as an OS benefit. There will be no scenario where we will not accept OS benefit as an endpoint. We will always accept OS benefit as the endpoint.' (P3)

'Most of the time I will accept overall survival and improvement in quality of life as the only two endpoints.' (P10)

Only one participant expressed some concerns with a drug that has improved OS, because of the magnitude of OS and toxicity profile.

Table 3. Summary of qualitative themes and examples for PFS

Qualitative themes	Examples
Reasons against PFS	
1. Effect on Survival	'If medication is very expensive and is not covered by insurance then I prefer OS as an endpoint and PFS is not good enough for me in that situation.'
Reasons in support of PFS	
1. Cost	"For some of the second-line therapies that add up to the overall survival, many patients won't afford it…. So, in this situation, we try to give a drug which has a maximum progression-free survival benefit even if it does not reflect in overall survival." (P1). "I am happy to accept progression-free survival as a good enough endpoint if it improves the patient's quality of life and the cost of the drug (that is being approved) is less than the standard of care." (P6) 'If the medication is very expensive and is not covered by insurance then I prefer OS as an endpoint and PFS is not good enough for me in that situation.' (P7)
2. Impact of medical literature	"So, I wouldn't use PFS as an end point usually. But, when you are working in a corporate sector, and you have all these papers justifying progression-free survival I may use it." (P6)
Case by case basis	
1. Cost-effectiveness	'In situations where the PFS will cost enormously to impose a financial burden on the patient, there I choose OS over PFS. Treatment is cost-effective there I choose PFS.' (P16)
2. For rare cancers or lack of alternatives	"If I am in the third- or fourth-line setting or my regular options that I use are over or I am treating a rare cancer with limited treatment options, I may accept the 'progression free survival' as a good enough point. But not in routine things, not in a first line, second line setting, not when I have multiple options available." (P10)

'But maybe where it (OS) improves by a very small amount but is associated with very high toxicity, I would not accept it as a very good outcome.' (P25)

Magnitude of benefit and price of cancer drugs deemed acceptable in Indian context

Participants were next asked about the minimum magnitude of benefit that they would consider as 'good enough' in terms of offering meaningful benefit for their patients. Their answers ranged from 1.5 to 12 months with a median of 4.5 months (IQR, 3-6 months) as the minimum PFS gains expected of a cancer drug. For these gains, Indian oncologists considered a monthly price of 10 000 Indian Rupee (INR) (IQR, 6000-30 000 INR and range, 4000-60 000 INR) as justifiable price (120 USD, IQR, 72-360 USD, range, 48-720 USA).

With regards to OS, the respondents' answer ranged from 2 to 24 months as the minimum gains expected from a cancer drug. The median response was a gain of 4.5 months (IQR, 3-6 months), which was similar to the expectations of a drug that improved PFS. They were, however, willing to accept a higher monthly price for drugs that improved OS. For these gains, Indian oncologists considered a monthly price of 30 000 INR (IQR, 15 000-50 000 and range, 4000-75 000) as justifiable price (360 USD, IQR, 180-600 USD, range, 48-900 USD).

DISCUSSION

In this report, we present results of the first qualitative in-depth survey of oncologists from LMICs regarding their perception of surrogate endpoints, what constitutes meaningful clinical benefit, and price of cancer drugs that would be deemed justifiable for the given benefit. We discover several major themes that provide important clinical and policy lessons for policymakers both in LMICs and HICs. These include understanding of surrogate endpoints, judgment on what constitutes meaningful benefit, and problems with pricing of cancer drugs.

Surrogate endpoints have already been discussed in depth in the oncology literature, including their utility as well as limitations.[12,14,20,21] Most cancer drugs in recent years have been approved based on surrogate endpoints, despite these limitations.[20,22] Analysis for validation of surrogacy have been exercised, and regulators, policymakers, and academicians regularly debate on this topic on academic venues, including conferences and journal publications. Similarly, issues related to what constitutes meaningful magnitude of benefit and justifiable cancer drug prices have been debated. An important perspective on these debates, however, has been missing- those of oncologists, people prescribing cancer drugs and undertaking shared decision discussions with patients. To our knowledge, no previous study—either from LMICs or HICs—has systematically studied oncologists' perceptions on drug pricing, and only one survey from China has previously explored physicians' perceptions on surrogate endpoints and magnitude of benefit specifically in relation to breast cancer.[23] We attempted to fill that gap in literature through an in-depth qualitative interview of oncologists to understand the nuances of their decision-making in relation to these three major cancer policy issues: endpoint surrogacy, magnitude of benefit, and drug pricing.

First, we found that the majority of oncologists in India do not feel comfortable using (or do not often use) drugs based on RR or PFS and would prefer using drugs based on OS. They expressed concerns regarding drugs that only improved RR but did not translate to OS and expressed that reducing tumour size alone did not constitute clinical benefit to justify toxicities. Almost all oncologists who used drugs based on RR, however, justified their decisions assuming that tumour shrinkage led to improved QoL for patients, despite lack of any evidence to suggest that RR has any correlation with QoL gains. Thus, it is the putative positive impact on QoL that oncologists have been led to believe for them to offer these drugs to patients based on RR alone. Specially, in an LMIC where patients pay from

pocket, a misunderstanding of therapeutic potential can be harmful. Thus, we urge oncologists to verify QoL impact based on QoL data, and not presume them based on RR.

Oncologists in our study did not focus on price of drugs for discussion of RR, but this was the most important issue for PFS discussion. Several participants justified using PFS-based drugs because drugs with OS would cost more. Studies from HICs have shown, however, that cancer drug prices do not correlate with OS or PFS gains.[3,24] Studies from LMICs looking at such correlations are lacking. Similar to the rationale for RR, participants justified using PFS-based drugs due to the presumed improvement in QoL. This assertion, however, has been consistently refuted by studies.[25-27] Thus, the two main reasons for using drugs based on PFS- cost and QoL- are actually not supported by evidence. This highlights the need to develop more awareness about these surrogate endpoints and drug pricing.

Previous studies have shown how patients and the public do not understand the nuances of the term PFS. Studies have shown that the public misinterprets PFS to mean survival gains, and even after explanation that OS data are not available, 40% of people continue to believe that a drug improves OS despite having only PFS data.[28] In fact, PFS has been previously proposed to be renamed as progression-free interval to avoid these confusions.[29] In terms of trade-off, a study among Canadian patients has shown that a majority would decline a treatment with only PFS gains, irrespective of the magnitude of benefit, and 26% would accept it for some PFS benefit in the range of 3-9 months.[30] The 4.5 month median benefit in PFS expected by oncologists in our interviews is aligned with this expectation from patients. In addition, this is also aligned with the minimum survival gains expected for clinically meaningful treatment benefits under the ASCO and ESMO-MCBS thresholds. ASCO has recommended survival gains of 2.5-6 months as meaningful based on tumour types,[31] and ESMO-MCBS recommends survival gains of $>$3 months, $>$5 months, and $>$9 months, respectively, for diseases with baseline OS of $<$12, 12-24, and $>$24 months respectively.[32]

Our study has also revealed that even physicians can misinterpret PFS by presuming improving PFS led to improved QoL. While it seems intuitive that shrinking cancer should improve QoL, QoL is not simply a function of tumour size alone unless it involves key anatomic structures. QoL is also a function of drug toxicity, and thus shrinking cancer may not always translate to QoL benefits. Future studies are needed from HIC settings to understand the perception of oncologists, and from LMIC settings to understand patient preferences regarding these endpoints and prices.

Through this study, we were also able to set a benchmark for the minimum expected gains and prices of cancer drugs for oncologists to consider as justifiable in the Indian context. For drugs that improved PFS at least by 4.5 months, a median price of 120 USD per month (upper range, 600 USD per month) was considered justified, while a drug that improved OS by a similar magnitude could justifiably be priced three times as high (360 USD per month, upper range up to 900 USD per month). This is not the current price of drugs in India, which is far higher, but this is what is deemed justifiable for a drug that improved PFS or OS by at least 4.5 months. Currently, we doubt there is any new drug that would meet this criterion. Furthermore, although these 'justifiable monthly drug prices' for India may look cheap compared with drug prices in HICs, they are still unaffordable.[6] To put this into perspective, the gross national income (GNI) per capita for India in 2022 was $2390. Even the 'justifiable' annual price for a cancer drug that improves OS is almost double that of the GNI per capita. In addition, some responses also highlighted the conflict between clinical decision-making based on price of drugs versus efficacy. For instance, some oncologists would use a drug that improved only PFS if it cost less than the drug that would improve OS. Such trade-offs associated with financial toxicity is another challenge in cancer care in LMICs, that needs to be studied in more detail.[33]

It is also interesting to note that the theme of over-treatment towards the end of life is an important issue not only in HICs but also in LMICs. In our study, one of the reasons for using drugs based on surrogate endpoints was the notion to do something for the patient when other options were exhausted. Thus, for LMIC policy planning, not only lack of access to drugs but also overtreatment should be accounted for. Indeed, Indian oncologists in our study also revealed the pressure they face to use some low-value therapies due to the drugs being Food and Drug Administration (FDA) approved and normalization of surrogate endpoints by the regulators and medical literature. This reinforces the notion that FDA approval status is applicable not only to the United States health care system, but can also have implications to policy and practice across the world.[34] For instance, one of our respondents specifically mentioned 'Sadly, FDA has made this as an endpoint, and our chemotherapy or post-surgery treatment is guided by the pathological complete response rate.' Another respondent argued that they had to use drugs based on PFS gains because their counterparts in HICs were using these drugs. This speaks to the need for LMIC cancer policymakers to be cognizant of the need for prioritization of cancer drugs based on local need and not be influenced by practice patterns of HICs.

Some limitations apply to our study. First, the sample size is relatively small. For a single nation study, however, we believe this is adequate especially given the saturation in themes. Second, the participants were selected through contacts of contacts, and thus, may have some bias. We did, however, receive different ranges of opinions. Third, physicians' responses included some misunderstanding of RRs and PFS (such as, equating them with QoL improvement), however, that represents a feature and not a bug of the study. We believe this misunderstanding that improving RR or PFS leads to better QoL is a pervasive misunderstanding even among physicians across the world and recommend conducting a similar study in HIC settings. Fourth, the majority of our respondents (76%) were male. At present, women constitute a large proportion of undergraduate medical students. The gender balance, however, is altered

as one approaches higher speciality training, such as medical oncology. Thus, we believe the gender representation in our study reflects the actual oncology workforce in India.[18] For the quantifiable variables such as median PFS, OS, and drug prices, the responses of female oncologists did not differ substantially from those of the male oncologists in our sample.

In summary, our study has shed light on physicians' perspectives regarding surrogate endpoints, their utility, minimum magnitude of clinical benefit deemed acceptable, and price of cancer drugs reasonable for those benefits. Our study provides a much-needed oncologists' perspective on these policy issues and establishes a benchmark of benefit and pricing expectations for cancer drug policy in LMIC settings.

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DISCLOSURE

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