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# Communication about the Risks and Benefits of Phase I Pediatric Oncology Trials

**Rebecca A. Hazen, PhD**[a], **Stephen Zyzanski, PhD**[b], **Justin Baker, MD**[c], **Dennis Drotar, PhD**[d], and **Eric Kodish, MD**[e]

[a]Department of Pediatrics, Case Western Reserve University and Rainbow Babies and Children's Hospital, 10524 Euclid Ave, Cleveland, OH, 44106, rebecca.hazen@uhhospitals.org

[b]Department of Family Medicine, Case Western Reserve University, 11100 Euclid Ave, Cleveland, OH 44106, sjz@case.edu

[c]St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105-3678, justin.baker@stjude.org

[d]Department of Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnett Ave, Cincinnati, OH 45229-3026, dennis.drotar@cchmc.org

[e]Center for Ethics, Humanities, and Spiritual Care, Cleveland Clinic, 9500 Euclid Ave JJ60 Cleveland, OH, 44195, kodishe@ccf.org

## Abstract

**Introduction—**Phase 1 pediatric oncology trials offer only a small chance of direct benefit and may have significant risks and an impact on quality of life. To date, research has not examined discussions of risks and benefits during informed consent conferences for phase 1 pediatric oncology trials. The objective of the current study was to examine clinician and family communication about risks, benefits, and quality of life during informed consent conferences for phase 1 pediatric oncology trials.

**Methods—**Participants included clinician investigators, parents, and children recruited from 6 sites conducting phase 1 pediatric oncology trials. Eighty-five informed consent conferences were observed and audiotaped. Trained coders assessed discussions of risks, benefits, and quality of life. Types of risks discussed were coded (e.g., unanticipated risks, digestive system risks, death). Types of benefits were categorized as therapeutic (e.g. discussion of how participation may or may not directly benefit child), psychological, bridge to future trial, and altruism.



Corresponding Author and Reprints: Rebecca A. Hazen, Ph.D., Department of Pediatrics, Case Western Reserve University, Rainbow Babies and Children's Hospital, 10524 Euclid Ave, Cleveland, OH, 44106, Phone: 216-844-3230, rebecca.hazen@uhhospitals.org.



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**Results—**Risks and benefits were discussed in 95% and 88% of informed consent conferences, respectively. Therapeutic benefit was the most frequently discussed benefit. The impact of trial participation on quality of life was discussed in the majority (88%) of informed consent conferences.

**Conclusion—**Therapeutic benefit, risks, and quality of life were frequently discussed. The range of information discussed during informed consent conferences suggests the need for considering a staged process of informed consent for phase 1 pediatric oncology trials.

## Keywords

ethics; informed consent; phase 1 trials

Participation of children in phase 1 oncology trials has raised a number of ethical questions and debates [1,2]. The primary scientific purposes of phase 1 pediatric oncology trials are *not* to test the efficacy of cancer drugs but rather to establish the maximum tolerated dose (e.g. safe dose) for cancer drugs, which can then be tested in phase 2 trials [3]. Thus, the balance of risks and benefits for the individual child is one of the primary ethical concerns [3]. Although phase 1 pediatric oncology trials offer only a small likelihood of direct benefit to the patient (average response of 5–10%) [4,5], phase 1 trials for pediatric cancers are typically approved by institutional review boards under the federal category “greater than minimal risk but presenting the prospect of direct benefit to individual subjects” (Part 46.405 Subpart D) [3]. Despite these circumstances, little is known about how clinicians and families communicate about the risks and benefits of pediatric phase I trials. Furthermore, recent ethical debates regarding risks and benefits from a study of premature infants [6,7] suggests the importance of obtaining data on discussions between research clinicians and families about these topics.

Parents rate communication with treating clinicians as important in deciding about phase 1 trials [8]. Research on parental decision-making about phase 1 oncology trials suggests that parents often perceive a variety of benefits of participation, including altruism, prolonging life, and curing their child’s cancer [9]. The impact of participation on quality of life (QOL) is also considered to be an important factor when considering participation in phase 1 clinical trials [10]. Effective communication about risks and benefits of participation in phase 1 clinical trials is thought to be complicated by “therapeutic misconception,” which refers to the belief that the purpose of research is to directly benefit the individual patient [11]. This is common for participants in clinical trials [12–14]. Given the existence of the therapeutic misconception, the small chance of direct benefit to the individual patient, and the potential risks, communication about risks, benefits, and QOL during informed consent conferences (ICCs) is of particular importance.

To our knowledge, research has not yet examined how clinician investigators and families communicate about risks and benefits during ICCs for phase 1 pediatric oncology trials. Using observational methods, the primary goal of the current study was to examine clinician investigator and family communication about risks, benefits, and impact of participation on QOL during ICCs for phase 1 pediatric oncology trials. A secondary goal was to examine

observer ratings of the quality of clinician investigator communication about risks and benefits.

## Methods

### Recruitment & Study Procedures

Data for the current study were collected as part of a multi-site project examining communication about phase 1 pediatric oncology trials across six research sites, which were chosen based on their participation in phase 1 pediatric oncology trials [15–19]. Institutional review board (IRB) approval was obtained at Cleveland Clinic (coordinating site) and the six data collection sites.

Inclusion criteria were that the family was considering participation for the child in an open phase 1 pediatric oncology trial and spoke either English or Spanish. Families who spoke other languages were excluded due to difficulty with translating study instruments. Pediatric oncology trials were defined as Phase 1 trials that enrolled individuals ages 22 and under with any cancer diagnosis.

Members of the healthcare team obtained permission from families for a research assistant (RA) to contact them. Prior to the ICC, RAs obtained written consent from participating physicians, parents, and patients age 18 or above. Assent was obtained for children between 7 and 17 years old. One hundred six families were approached regarding participation in the study, 85 families (80%) consented to allowing the ICC to be observed and audiotaped, and 60 of these families agreed to be interviewed after the ICC. Data from the parent interview were previously reported [15,16,18]. Demographic and disease information for those who declined participation in the current study was not available.

ICCs were silently observed by RAs, who digitally audio recorded the ICCs. Participants in ICCs included clinician investigators, patients, and family members.

### Measures

**Demographics—**The following demographic information about parents and patients was collected from parents during parent interviews: age, gender, education, occupation, race, religious preference, and number of additional children. The Hollingshead Index of Social Position (ISP) [20] was calculated based on occupation and education and was used to measure socioeconomic status (SES), with lower ISP scores indicate higher SES. Demographic data about clinician investigators was obtained from the General Clinician Questionnaire, which was designed by study investigators [19]. Clinician investigator demographics included age, gender, race and number of years caring for children with cancer.

**Communication During ICCs—**Audiorecorded ICCs were coded using the ENCOUNTER Codebook, which was created based upon rulebooks that were used in previous studies [21,22]. The rulebook included detailed instructions, definitions of terminology, and examples of communication to guide raters. ENCOUNTER, a Web-based health communication analysis software program, was used to code the audio recordings

using the ENCOUNTER Codebook. The following data on risks/side effects was coded: whether risks/side effects were discussed, who raised the topic of risks/side effects (every occurrence during ICC was coded), whether the clinician investigator described risks/side effects of participation, and the types of risks discussed (e.g. digestive, sleep/fatigue; see Table 1 for risk categories). The types of benefits discussed were also coded. Type of benefits included therapeutic (e.g. tumor shrinkage), psychological (e.g. feeling like they are not "giving up"), altruism (e.g. helping future children with cancer), and bridge to another clinical trial (e.g. participating to get some benefit that will allow participation in another trial). It should be noted that discussion of therapeutic benefits were coded as occurring regardless of whether the clinician investigator indicated that the child would be likely to receive direct therapeutic benefit. For example, the small chance of direct benefit could be highlighted by the clinician investigator. We attempted to further code therapeutic benefit based on the whether the discussion emphasized low, moderate, or high likelihood of benefit. However, it was not possible to reliably code discussion of the likelihood of benefit due to the high level of nuance and ambiguity in these discussions (e.g. "hope it slows down the tumor but there is no guarantee," "don't know if it works….hope it works," "'it's promising but not proven….no promise it will work"). It is noteworthy that none of the ICCs included clinician investigators discussing the phase 1 study as being likely to cure the cancer. Finally, clinicians' effectiveness of communication about risks and benefits were rated by trained RAs on a 10 point Likert scale, with 1 representing poor communication and 10 representing optimal communication. Higher scores were given for more complete discussions of risks and benefits. To receive a high score on this rating scale, the clinician had to explain the types of risks and benefits and not just list side effects or briefly mention benefits.

Discussions about QOL (positive, negative, or neutral) and impact of trial participation on extracurricular activities (e.g. school, sports, social life) were coded as to whether they occurred (e.g. increasing or decreasing symptoms, changes in child's daily activities) and who raised the topics. The first author also coded the discussions about QOL as to whether they were positive, negative, or neutral.

Given that information on risks and benefits is also provided in the informed consent documents (ICD), ICDs were also coded to examine how frequently the types of risks and benefits described above were presented in the ICDs. Specifically, the types of risks (see Table 1) and benefits (e.g. therapeutic, psychological, bridge to future trial, altruism) described in the ICDs were coded.

Training for coders of ICCs included 60 hours of training over a four-week period, during which coders were trained on how to identify specific communication topics. Inter-rater reliability was examined by double coding 30% of ICCs. Kappa correlations for the categorical clinician investigator behaviors coded using ENCOUNTER and examined in the current study ranged from .85–1.0 [23].

### Statistical Analysis

Descriptive statistics were computed, with means and standard deviations used for continuous variables and percentages used for categorical variables. Ninety five percent confidence intervals were also computed for all risk categories coded as a percent.

## Results

### Patient and Parent Demographics

Patient and parent demographic information was available for 60 families who completed the parent interview and have been reported by Cousino and colleagues [15]. The majority of patients were male (n = 54; 63%) and the average age of patients was 11 years (SD=5.5; range = 1–21 years). The most common diagnoses were brain and CNS tumors (n = 28; 33%) and bone or soft tissue cancer (n = 26; 31%). Additional cancer diagnoses included neuroblastoma (n=17; 20%), leukemia (n=7, 8%), and other less common cancer diagnoses (n = 7, 8%). The majority of phase 1 protocols that participants consented to were receptor/signal transduction studies (i.e. kinase inhibitors; 20/33, 61%), 7 (21%) were cytotoxic chemotherapy studies, 5 (15%) were immunodulator studies (e.g. antibody agents), and one was an angiangiogenesis study. Sixty five (76%) of the 85 patients had expired at the time of the current analyses, with an average of 254 (SD = 229.3, range = 17 – 981) days from the ICC to the patient's death. Parent participants were predominantly female (n = 43; 72%), represented the racial majority (n = 51; 85%), and had an average age of 42 years (SD = 8.2; range = 23–66 years). Socioeconomic status was equally distributed amongst the low (n = 21; 35%; ISP = 4–5), medium (n= 20; 33%; ISP=3), and high (n = 19; 32%; ISP=1–2) groups on the ISP.

### Clinician Investigator and Conference Characteristics

Clinician investigator and conference characteristics were reported previously [15]. Clinician investigators had been caring for children with cancer for an average of 14 years (SD=8.1) and had an average age of 44 years (*SD*=6.8) [15]. Fifty-four percent of clinician investigators were female and 15% were racial/ethnic minorities. A nurse participated in 40% of ICCs. On average, the ICC lasted 45 minutes (*SD*=20) and there was an average of 5 (SD=1.2) participants in the ICCs. Patients were present in 98% (83/85) of ICCs. The ICD was provided in 69% of ICCs and signed during 66% of ICCs. Ninety-five percent of families agreed to enroll their child in a phase I study.

### Clinician Investigator-Family Communication About Risks and Benefits

Risks were discussed 271 times in 95% of ICCs (81/85). An examination of conference and demographic characteristics did not reveal differences for the four ICCs in which risks were not discussed versus those in which there was discussion of risks. Clinician investigators raised the topic of risks 75% (204/271) of the time. In addition, parents and patients raised the topic of risks 20% (53/271) of the time and 5% (14/271) of the time, respectively. The types of risks discussed are presented in Table 1. The most frequently discussed risks included digestive risks (80% of ICCs) and hematological/oncologic risks (67% of ICCs). As shown in table 1, the least frequently discussed risks included loss of confidentiality

(1.2% of ICCs), immune system risks (8% of ICCs), and risks related to medical procedures (10% of ICCs). Death was discussed as a risk in 9% of ICCs. Fifty three ICDs were used across the six research sites and most risks were presented more frequently in ICDs than during ICCs (Table 1).

Benefits were discussed in 88% (75/85) of ICCs. Therapeutic benefits were discussed 160 times in 85% (72/85) of ICCs and were raised by clinician investigators 84% of the time (134/160) and patients/families 16% (26/160) of the time. Psychological benefits were discussed 7 times in 7% (6/85) of ICCs, with 71% (5/7) of these discussions being initiated by clinician investigators and 29% (2/7) of discussions initiated by families. Discussion of altruism as a benefit of participation occurred 51 times in 41% (35/85) of ICCs. Altruism discussions were raised predominantly by clinician investigators (75%, 38/51). Discussion of participation in the clinical trial as a bridge to extend life for subsequent research occurred 13 times in 13% (11/85) of ICCs and this was raised primarily by clinician investigators (11/13; 85%). Parents/family raised the topic of a bridge to another trial 15% (2/13) of the time. Examples of discussions about risks and benefits are provided in Table 2.

With regard to presentation of benefits in ICDs, all of the ICDs presented therapeutic benefits and altruism as benefits of participation. However, psychological benefits and participation as a bridge to extend life for subsequent research were not presented in any of the ICDs.

### Ratings of Clinician Communication About Risks and Benefits

Ratings of clinician communication about risks and benefits ranged from 1 to 9, with a mean of 5.98 out of 10 (SD=1.65, n=85). As shown in Figure 1, the data was skewed, with only 15% of ratings falling below five. Ratings of risks and benefits communication did not differ significantly based on whether a nurse was present during the ICC ($t = .83$, $p = .41$).

### Clinician Investigator-Family Communication About QOL

The potential impact of participation on child QOL was discussed 149 times in 88% (75/85) of ICCs. Clinician investigators raised the topic of QOL 71% (106/149) of the time and patients and families raised the topic 29% (43/149) of the time. Discussions of the impact of participation on QOL were predominantly neutral (74/149; 50%) or negative (60/149; 40%), with only 10% (15/149) of discussions being positive. In addition, the potential impact of participation on extracurricular activities was discussed 23 times in 21% (18/85) of ICCs. Families and patients raised the topic of extracurricular activities 70% of the time (18/23) and clinician investigators raised the topic 30% of the time (7/23). Table 2 provides examples of communication about QOL and impact on extracurricular activities.

## Discussion

The current study provides the first data from directly observed audio-taped communication about risks, benefits, and QOL during ICCs for phase 1 pediatric oncology trials. Results indicated that discussion of risks and benefits were common during ICCs, with risks discussed in 95% of ICCs and benefits discussed in 88% of ICCs.

Given the concerns about families being able to balance the risks and benefits of participation in phase 1 studies [1–3], it is encouraging that the overwhelming majority of ICCs contained discussion about both risks and benefits. Although clinician investigators most frequently raised the topics of risks and impact on QOL, both parents and children also raised the topics during the ICCs, suggesting that families are seeking necessary information prior to deciding on participation. Research by Maurer and colleagues [10] indicated that parents who identified QOL concerns were less likely to consent to enrolling their child in a phase 1 trial. In the current study, QOL discussions ranged from negative to positive and 95% of families consented to enrollment in a phase 1 trial. It is important for additional research to examine how discussions about QOL in ICCs may impact decision making about phase 1 trials.

A wide variety of risks were discussed during ICCs, with digestive and hematological/oncologic risks discussed the most frequently. Despite the fact that phase 1 studies always present a chance for unanticipated risks, approximately 65% of ICCs did not include a discussion of unanticipated risks. Although risks were frequently discussed during most ICCs, the results suggest that there are important risks of participation in phase 1 trial that are frequently omitted. However, coverage of risks by clinician investigators during ICCS is also likely to be influenced by coverage of risks in the ICDs, which tended to be extensive in the current study.

In the current study, death was discussed as a risk of participation in 9% of cases. It is important to consider whether pediatric oncologists should discuss the risk of death from phase 1 studies. Although death is clearly the most serious outcome, the low rates of death related to drug toxicity in phase 1 pediatric oncology trials (0.5–0.7%) [4,5] may lead clinician investigators to conclude that it is not necessary to discuss this risk. Additionally, clinician investigators may be concerned that discussion of the risk of death due to trial participation could be confused with the risk of death related to the disease. It should be noted that discussions about death related to the disease were not coded as a risk of trial participation and data from this project suggest that discussions about death related to incurable disease occured in approximately 15% of ICCs [24]. Additional research is needed to investigate families' preferences for such information and may provide guidance to pediatric oncologists on how to balance discussion of risk of death from incurable disease with risk of death from the phase 1 study.

The most frequently discussed benefit was therapeutic benefit. The presence of discussions about therapeutic benefits did not necessarily mean that clinician investigators were promoting trial participation. There was variability in discussions (see Table 2 for examples), with many clinician investigators highlighting the inability to predict whether there would be any therapeutic benefit. Qualitative studies of parental decision making suggest that therapeutic benefit is a primary concern when considering participation for their child in a phase 1 study [9]. Additionally, research on adult patients with cancer indicates that therapeutic benefit is their chief reason for participating in phase I trials [25]. Thus, despite the low probability of therapeutic benefit, it is not surprising that this was the most frequently discussed benefit. However, altruism and psychological benefits (e.g. feeling good about having something to fight for) were also discussed during ICCs. Additional

research is needed to assess whether patients and/or their families perceive psychological benefits after participating in phase 1 trials.

It is noteworthy that psychological benefits were raised predominantly by families and discussion of other benefits and risks were primarily initiated by clinician investigators. Differences in the topics raised by families and clinician investigators may reflect differences in the perceived value of phase 1 studies for pediatric cancers. Consistent with this notion, research by Mack and colleagues [26] indicated that parent rating of quality of care at the end of life was associated with physician care and sensitivity in communication but physician ratings of the quality of care provided was associated with ratings of pain and days spent in the hospital. Taken together, these results suggest that it is important to better understand families' preferences and values for the care for children facing end of life decisions. Additionally, given the unexpectedly high rate of child presence during the ICC, it is also important for future research to better understand the child's views on communication about risks and benefits. It is not clear if child presence influenced discussions about risks and benefits but information on the child's perspective about these discussions may help to guide decisions about coverage of these important topics.

It should be noted that clinician investigators are faced with the task of explaining a variety of complicated concepts, such as maximum tolerated dose and dose-limiting toxicities [15], along with the standard elements of informed consent. Some of these aspects of informed consent are more general (e.g. confidentiality, right to withdraw), and others, such as risks and benefits, are quite nuanced for a phase 1 study. However, data from a recent survey of pediatric oncologists and fellows indicates that only 21% received formal training in communication about these topics [19]. These data suggest that hematology/oncology programs that feature Phase I initiatives should integrate training in communication about informed consent for phase 1 studies as a key component of their efforts.

The finding that the average rating of the quality of clinician communication about risks and benefits was approximately a 6/10, indicated an area for improvement in discussions about phase 1 trials. Research has supported the use of question prompt lists during the informed consent process [27,28] and they may be particularly useful for complex studies, such as phase 1 trials. Additionally, our previous research on informed consent for phase 3 pediatric oncology trials has supported the use of a staged consent process model [22,29] in which certain key topics are covered prior to introducing topics related to the particular trial. The quantity and complexity of information to be discussed during ICCs for phase 1 trials suggests that a similar approach may be helpful. Data on family preferences for the informed consent process from a subset of participants in the current study indicated a preference for more information on topics such as risks and benefits and more time to weigh options and ask questions, which provides further support for having multiple ICCs with specific goals for each ICC [30]. As part of ongoing research, we are currently evaluating family preferences for how to best use a two-step process of informed consent.

Limitations of the current study include that it is possible that conversations about phase 1 trials occurred outside of the ICCs and were not assessed. For example, patients who traveled to a study site for the purposes of enrolling in a phase 1 trial may have discussed the

trial with a treatment provider at another institution. The rating of the discussions about risks and benefits must be interpreted in light of this limitation. Additionally, the rating of the communication about risks and benefits assessed how completely risks and benefits were discussed but did not account for more qualitative aspects of communication, such as warmth and engagement of the clinician investigator with the family. It may be that families value these more qualitative aspects of communication more than completeness of communication. Finally, although study sites were selected based on high levels of phase 1 research activity, clinician investigators and patients from these sites may not be representative of individuals at other sites. For example, the sample predominantly represented the racial/ethnic majority and future research is needed with more racially/ethnically diverse samples.

Strengths of the study include that consent conversations were observed and coded rather than relying on reports from participants as to topics covered during the ICCs. The use of this methodology eliminates difficulties related to recall of consent conversations. Additionally, the sample was diverse with regard to socioeconomic status and cancer diagnoses, which increases the generalizability of the results.

The current study supports the value of assessing communication during ICCs for families considering participation for their child in a phase 1 study. Although risks, benefits, and quality of life were frequently discussed during ICCs, future research is needed to test models for *how* to discuss these important aspects of clinical trials as well as methods for better coding explanation of benefits during communication. Research is also needed to examine models for discussing the risk of death in clinical trials. Finally, research with other patient populations is needed to assess the extent to which findings may generalize to other types of phase 1 studies.

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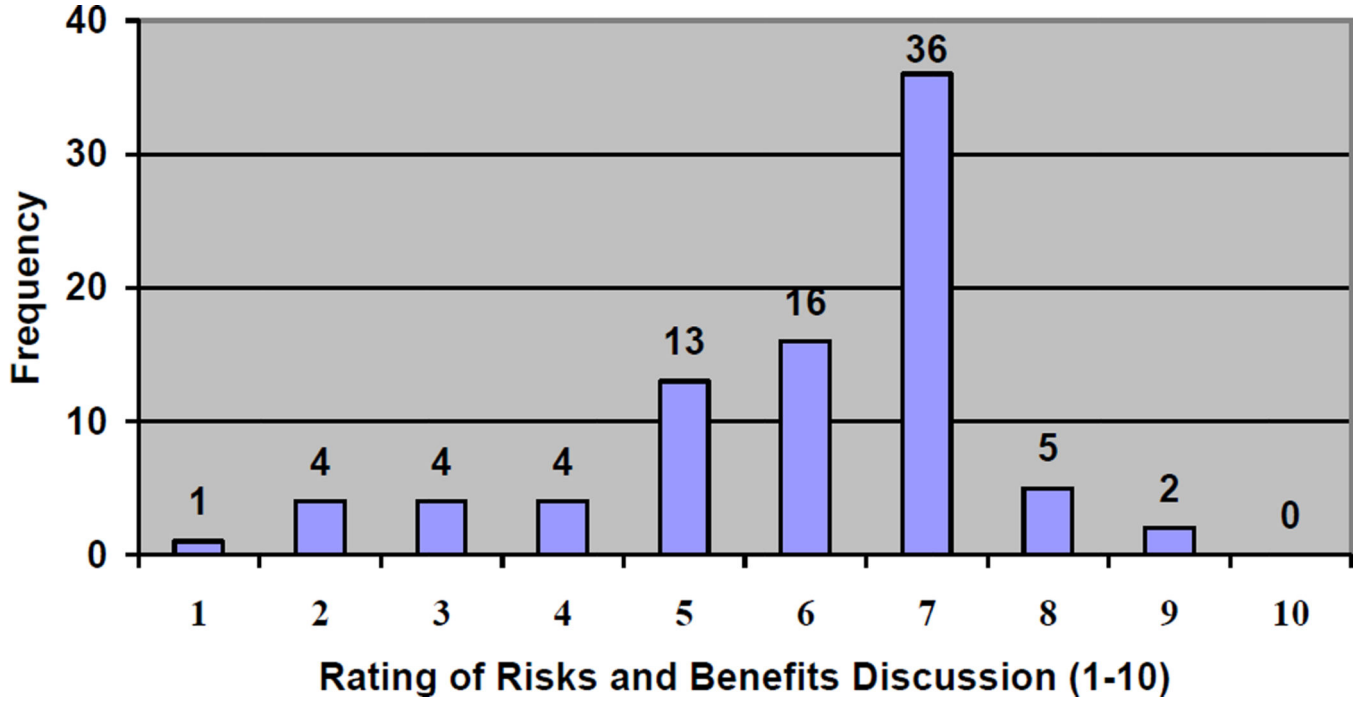


**Figure 1.**

Observer Rating of Risks and Benefits Discussions

Ratings of risks and benefits discussions are based on a 1–10 scale, with higher scores indicating a more balanced presentation of risks and benefits.

## Table 1

Types of Risks Discussed During ICCs

| Risk Categories | Examples | % of ICCs (n) (95% C.I.) | % of ICDs (n) (95% C.I.) |
|---|---|---|---|
| GI/digestive | nausea, vomiting, diarrhea, decreased appetite, liver irritation/ inflammation, increased liver tests | 80.0% (68) (±8.5%) | 100% (53) (±0%) |
| Hematology/Oncology | Bleeding, change in blood counts, blood clots, neutropenia, bleeding inside tumor, bone marrow suppression | 67.1% (57) (±10.0%) | 96.2% (51) (±5.1%) |
| Integumentary | hair changes (color, loss), hand and foot syndrome, rash, dry skin, peeling of hands and feet | 65.9% (56) (±10.1%) | 98.1% (52) (±3.7%) |
| Sleep/Fatigue | Fatigue, tired, knocked down, lethargy, sleepiness, decreased energy, weakness, malaise, bad sleep | 57.7% (49) (±10.5%) | 92.5% (49) (±7.1%) |
| Cardiovascular | high blood pressure, heart failure, heart attack, increased heart rate | 43.5% (37 (±10.5%) | 90.6% (48) (±7.7%) |
| Pain/Tingling | tingling (in hands and feet), numbness, burning, general and specific pain (e.g. headache, joint pain) | 40.0% (34) (±10.4%) | 96.2% (51) (±5.1%) |
| Unanticipated | Things don't know, unknown/unexpected side effects, don't know safety, | 35.5% (30) (±10.2%) | 96.2% (51) (±5.1%) |
| Reproductive System | risk/damage to fetus, not allowed to father children, fertility problems | 35.3% (30) (±10.2%) | 92.5% (49) (±3.7%) |
| Nervous System | dizziness, balance difficulties, encephalopathy, seizures | 32.9% (28) (±10.0%) | 84.9% (45) (±9.6%) |
| Flu-like Symptoms | Fever, flushing, cough, sweating, chills, runny nose | 29.4% (25) (±9.7%) | 83.0% (44) (±10.1%) |
| Musculoskeletal | muscle breakdown/weakness, muscle cramps, abnormal bone growth, abnormalities of bones | 28.2% (24) (±9.6%) | 79.2% (42) (±10.9%) |
| Urinary System | kidney failure/, bladder irritation, decrease protein stores, increased protein excretion, | 24.7% (21) (±9.2%) | 83.0% (44) (±10.1%) |
| Respiratory System | shortness of breath, airway obstruction, inflammation of lungs, lung disease | 24.7% (21 (±9.2%) | 84.9% (45) (±9.6%) |
| Eating/Oral | dry mouth, taste aversion, parestesia, dysthesia, mouth and esophagus sores | 23.5% (20) (±9.0%) | 67.9% (36) (±12.6%) |
| Chemical Imbalances | salt, sodium, potassium, calcium, phosphorus, magnesium, electrolyte abnormalities/levels | 23.5% (20) (±9.0%) | 71.7% (38) (±12.1%) |
| Infections | blood infections, viral/bacterial infection | 23.5% (20) (±9.0%) | 75.5% (40) (±11.6%) |
| Allergic Reactions | allergic reaction to antibody, drug reaction | 22.4% (19) (±8.9%) | 52.8% (28) (±13.4%) |
| Vision | night blindness, floaters in eye, blurry vision, vision changes | 20.0% (17) (±8.5%) | 69.8% (37) (±12.4%) |
| Mood/Behavior or Mental Status | suicidal ideation, calmness, behavior change, mood changes, confusion, hallucinations | 17.7% (15) (±8.1%) | 69.8% (37) (±12.4%) |
| Swelling/Fluid Changes | swelling in arms/legs, fluid retention | 15.3% (13) (±7.7%) | 77.4% (41) (±11.3%) |
| ENT | hoarse/whispery voice, change in voice, ears, nasal, hearing, throat sensations | 12.9% (11) (±7.1%) | 47.2% (25) (±13.4%) |
| Endocrine System | change in blood sugars, diabetes, pancreas inflammation/irritation | 12.9% (11) (±7.1%) | 75.5% (40) (±11.6%) |
| Negative Consequences Due to Dose of Drug | dose limiting toxicity, toxicity of drug | 11.8% (10) (±6.9%) | 3.8% (2) (±5.2%) |

| **Risk Categories** | **Examples** | **% of ICCs (n) (95% C.I.)** | **% of ICDs (n) (95% C.I.)** |
|---|---|---|---|
| Second cancer | other tumors or cancers | 10.6% (9) (±6.5%) | 26.4% (14) (±11.9%) |
| Weight Change | increased weight, weight loss, change in weight | 10.6% (9) (±6.5%) | 54.7% (29) (±13.4%) |
| Risks Related to Other Medical Procedures | transfusion risks (e.g. HIV), blood draw risks | 10.6% (9) (±6.5%) | 79.2% (42) (±10.9%) |
| Death | death, life threatening side effect | 9.4% (8) (±6.2%) | 88.7% (47) (±8.5%) |
| Immune System | immune suppression, immune reaction | 8.2% (7) (±5.8%) | 24.5% (13) (±11.6%) |
| Other | financial, inconvenience, impact on daily activities | 4.7% (4) (±4.5%) | 18.9% (10) (±10.5%) |
| Loss of Confidentiality | ---- | 1.2% (1) (±2.3%) | 7.5% (4) (±7.1%) |

**Table 2**

Example of Communication About Risks, Benefits, and QOL

| Topic | Communication During ICCs |
|---|---|
| Benefits | |
| Therapeutic | **1** Clinician Investigator: "The benefit may be that the disease will get better or stabilize. I think that the likelihood that it will go completely away is very small."<br>**2** Clinician Investigator: "Hope it's going to help you…don't know that"<br>**3** Parent: "Does it eliminate the cancer cells? Clinician: "We don't know."<br>**4** Clinician Investigator: "We know that there have been rare…but some kids have had a response, more likely stable disease with this medicine." |
| Psychological | **1** Parent: "I want this to be hope for him, try this and say let's give it a go"…Clinician: "It's painful to go through every possible side effect…on the other hand, some people would find it painful not to try any new medicines…I can't make that decision for you."<br>**2** Clinician Investigator: "I think you've known from the beginning that she has an incurable disease that we are trying to defy odds with and that's what this about." |
| Altruism | Parent: "Do you want to do the spinal tap? Child: "If it will help the study, I will"…. Clinician: "It will not benefit you, it will benefit the study." |
| Bridge To Future Trial | Clinician Investigator: "If she is benefiting from this drug, she would take it for a year according to the study…I don't anticipate she would be on it for a year…I think at some point we would want to get her to immunotherapy." |
| Risks | Clinician Investigator: "It has side effects and side effects are not dissimilar to other chemotherapies…This is obviously an important part for us to spend some time on." |
| Quality of Life | |
| Positive | Clinician Investigator: "Part of this is maintaining her quality of life as much as possible." |
| Neutral | Patient: "Do I have to get up at 3:00 in the morning to do weight and height?"<br>Clinician Investigator: "No, you don't have to do that." |
| Negative | Clinician Investigator: "Behind the shield is the key thing, is that we need you behind the shield and you know we will help you get through this." (in reference to contact restrictions) |
| Extracurricular Activities | Parent: "My concern for her is there is two things that she does that she absolutely loves, there is dance and school…<br>Clinician Investigator: "Yep, the goal is for her to do those things and for you to not notice any difference." |