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ORIGINAL RESEARCH

Attitudes Toward Discussing Approved and Investigational Treatments for Cystic Fibrosis in Prenatal Genetic Counseling Practice

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Abstract This project aimed to explore the attitudes of prenatal genetic counselors toward discussion of novel approved and experimental CF treatments in the prenatal setting, and to assess how knowledge of genotype-specific, targeted treatments may influence their current practices. Targeted treatments have the potential to impact the health-related quality of life of individuals affected with CF and therefore, knowledge of the availability of such treatments may influence the decision-making process of parents who receive a fetal diagnosis of CF. Using the 2012 FDA approval and introduction of ivacaftor into CF clinical practice as a case study, a survey was designed to explore the opinions and practices of prenatal genetic counselors with regard to counseling for a prenatal diagnosis of CF, and how those practices might be impacted by the availability of a new genotype-specific treatment. Approximately 800 genetic counselors were sent questionnaires in January of 2013. Respondents were provided information about this treatment and were asked to rate its perceived benefits, along with the likelihood that they would discuss potential benefits and limitations with parents receiving a prenatal diagnosis of CF. One-hundred sixty-nine prenatal genetic counselors (21.1 %) responded to the survey. Results indicated that 80 % of respondents 'never heard of the drug', or they were 'not exactly sure' what it was. After reading the materials provided, counselors felt the new treatment would have 'some' or a 'significant' impact on an affected individual's life. Their opinions varied on what information about this treatment they would choose to discuss with their patients; even if the treatment is currently FDA approved and clinically available for affected individuals with the genotype of the fetus. However, they would 'definitely' refer these patients to a specialist to discuss targeted treatments further. Most prenatal genetic counselors indicated there are certain scenarios in the prenatal setting which warrant a discussion of targeted treatments for CF, at least on some level. Counselor's views on sharing information about new treatment options are shaped by their familiarity with the treatment and their perception of its benefits and limitations, their comfort discussing these subjects, and their interpretation of the genetic counselor's role. Most genetic counselors had never heard of ivacaftor or Kalydeco™ prior to taking the survey. Therefore, counselors need to be better educated about the availability of CFTR mutation-based treatments before they will be able to incorporate discussion of new treatment options into their counseling.

Keywords Cystic fibrosis · Personalized medicine · Targeted treatments · Ivacaftor · Prenatal genetic counseling

Population-based prenatal screening programs for cystic fibrosis (CF) began in the US in 2001, and screening is now routinely offered to pregnant women and to women planning a pregnancy (ACOG 2011). In the event of identification of a pregnancy at risk for CF, or with a positive prenatal diagnosis, genetic counselors may be the first to provide prospective parents with an overview of the condition, including general information about available treatment and management options. The goals of this project are to explore prenatal genetic counselors' attitudes toward and awareness of newly approved and experimental CF treatments that target the underlying cause of CF, and assess to what extent genetic counselors would consider incorporating

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information about these types of treatments into their current prenatal counseling practices.

Cystic Fibrosis (CF)

CF is the most common life-threatening autosomal recessive condition among Caucasians (Barrett et al. 2012), with a frequency of 1/3500 babies born in the United States (CFF, Cystic Fibrosis Foundation 2014). Although prevalence is highest in individuals with European ancestry, CF affects people from varied backgrounds and throughout the world (Bobadilla et al. 2002). CF in its classical presentation affects many organs, predominantly the lungs and pancreas, and is generally considered a severe, life-limiting condition. Patients with CF exhibit a wide range of symptoms and therefore experience different degrees of severity.

Treatment and Disease Management

Individuals living with CF follow a rigorous treatment regimen tailored to their specific symptoms. Treatment burden is high in terms of time, money, and energy. Dozens of drugs in the form of nebulizers, pills, and nasal sprays are incorporated into patients' daily routines (Flume and Van Devanter 2012). Medications are accompanied by thirty minutes to several hours of manual or mechanical airway clearance therapies each day to loosen mucus,expel it from the respiratory tract, and avoid lung damage. (Flume and Van Devanter 2012). Even with aggressive treatment, CF will eventually develop into end stage lung disease (Ratjen 2009). Receiving a lung transplant is an option for patients with advanced disease. Lung transplantation eliminates respiratory problems for the recipient but is not a cure.

Since the discovery of CF, earlier diagnosis in conjunction with the availability of more effective treatment options have contributed to slower disease progression and quality of life improvements. The median predicted lifespan of an individual with CF is now 40.7 years (CFF, Cystic Fibrosis Foundation 2014). People with CF are able to set and achieve major life milestones including education, marriage, and having children. Mental health issues including depression and anxiety are common (Abbott et al. 2015). Despite advances in the outlook for affected individuals, there is still no known cure for the condition.

Recently approved and experimental targeted treatments, also known as modulators, which address the basic defect of CF, may represent a significant step forward. These include ivacaftor (brand name Kalydeco™), a CFTR potentiator, which was FDA-approved in January of 2012. As of May 2015, ivacaftor is FDA approved for patients with specific CFTR mutations, including the G551D and eight additional "gating" mutations (G178R, S549 N, S549R, G551S, G1244E, S1251 N, S1255P and G1349D) that comprise approximately 4–5 % of CF patients (Yu et al. 2012; CFF2011) the R117H CFTR mutation (De Boeck et al. 2014), which comprise an additional 2.8 % of patients with CF in the US (CFF, Cystic Fibrosis Foundation 2014). There is no long-term data regarding improvements or side-effects. The cost of ivacaftor, estimated to be over $250,000 per year, may pose a significant barrier to obtaining this and other genotype-specific treatments (Balfour-Lynn 2014).

A combination of genetic modulators (ivacaftor/lumacaftor) targeting the common genotype F508del/F508del (Boyle et al. 2014) was approved by the FDA for patients 12 and older in July 2015, after this study was completed. Ataluren, a targeted treatment that leads to translational read-through of nonsense mutations is also in clinical trials (Kerem et al. 2014).

Presently, discussions about genotype-specific treatments are taking place in both pediatric and adult CF care settings. The extent to which these conversations occur in the prenatal setting is unknown (Massie et al. 2014). Awareness of new options and research may influence the decision-making processes of parents who receive a prenatal diagnosis of CF. While ivacaftor alone is effective for a minority of patients, its introduction stands as a model for other targeted treatments currently in development, and a harbinger of things to come.

Methods

Survey Development

An online survey was designed to explore the opinions and potential practices of prenatal genetic counselors with regard to a prenatal diagnosis of CF and how those practices might be impacted by the availability of a new targeted treatment. They were asked about the importance of prenatal counseling with respect to the affected individual's life expectancy, physical health, psychological & emotional health, social functioning & personal goal fulfillment, and treatment burden. The survey questions were based on a review of the literature and drawn from the clinical experiences of the investigators. Survey categories (except life expectancy) were drawn from the Cystic Fibrosis Questionnaire-Revised (CFQ-R), a validated survey widely used in CF clinical research, which was developed to measure health-related quality of life for adolescents and adults with CF (Quittner et al. 2005). The survey contains 44 questions which examine twelve different domains: physical functioning, body image, digestive symptoms, respiratory symptoms, emotional functioning, social functioning, eating disturbances, treatment burden, vitality, health perception, role functioning, and weight. The questionnaire is used by healthcare professionals in evaluating patients and by researchers in assessing the efficacy of new treatments. As expected, it has been found that disease severity is inversely

related to quality of life. Children with CF generally indicate a better quality of life than adults with CF (Cohen et al. 2011).

Pulmonary exacerbations have a profound negative effect on perceived quality of life in both physical and psychosocial domains of the CFQR (Britto et al. 2002). Other measures of health, such as lung function, have not been found to be associated with decreased perceived quality of life (Britto et al. 2002). Research has also shown that patients with more frequent pulmonary exacerbations score lower, on average, in all twelve domains measured by the CFQ-R (Bradley et al. 2013).

Survey

Counselors were presented with a hypothetical scenario in which a fetus was found to be affected with two F508del mutations. Questions were aimed to assess, using a five-point Likert scale, what prenatal genetic counselors perceive as the impact of CF on the five above-mentioned aspects of an affected individual's life. Participants also were asked to rate the likelihood that they would discuss each of these topics with the theoretical prospective parent.

After the initial mock scenario was presented, information on the case study drug, ivacaftor, (Kalydeco, referred to as "drug or targeted treatment" in this paper) was presented to study participants. A description of the drug was developed based on clinical trial results, product inserts, and patient testimonials from the media. Follow-up questions assessed each counselor's perception about the efficacy of this treatment and the likelihood that they would discuss potential benefits of the drug with a patient whose fetus was affected with one F508del mutation and one G551D mutation. Lastly, participants were informed about a treatment option currently in clinical trials for patients with F508del mutations, and queried as to the likelihood that they would discuss potential future treatments in a prenatal genetic counseling session when the fetus was affected with F508del mutations. Counselors' concerns about new treatments or treatments pending FDA approval were also assessed.

The survey was hosted by SurveyMonkey and took approximately 10–15 min to complete. Univariate results were analyzed in SurveyMonkey. Bivariate analysis and statistical tests were performed with version 22 of IBM SPSS Statistical software.

Sample

All genetic counselors currently practicing in a prenatal genetic counseling setting were eligible for participation. An email stating eligibility criteria and the general purpose of the study along with a hyperlink to the online survey was sent to all members of the National Society for Genetic Counselors (NSGC), which consists of approximately 800 prenatal genetic counselors (NSGC, National Society of Genetic Counselors 2012). Participants were notified that their responses were anonymous and that they were able to discontinue participation at any point during the survey.

A total of 169 genetic counselors responded, a response rate of approximately 21 %. Twelve participants answered only three initial demographic questions, so the final sample size was 157 respondents. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional (Sarah Lawrence College) research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

Professional Experience of Respondents

Participants had a wide range of experience in the prenatal genetic counseling field from less than 6 months to 32 years. The average amount of time spent practicing in a prenatal setting was 8.2 years and the median was 5 years. The average number of patients counseled regarding a diagnosis of CF was 5.4 and the median was 2.

Perception & Discussion of CF

Participants were presented with the first scenario prior to receiving any information about the targeted treatment. Participants were asked to envision a scenario in which they had identified a fetus affected with two F508del CFTR mutations. The respondents were asked to estimate the overall impact that CF would have on certain aspects of the affected individual's life on a rating scale of 1 (little or no impact) to 4 (profound impact). Counselors expressed the most concern about the impact on physical health (M = 3.39) and the least concern about social functioning and personal goal fulfillment (M = 2.29) (Table 1). With regards to the same scenario, participants were asked to rate the likelihood that they would address these impacts with the patient during a results session. The majority of counselors would 'definitely' discuss physical health (94.2 %), life expectancy (86.4 %) and treatment burden (70.8 %), while less than a quarter would 'definitely' discuss psychological and emotional health (22.7 %) or social functioning and personal goal fulfillment (24 %) (Table 2).

Correlations between the perception of the effect of CF on specific aspects of life and the likelihood of discussing these specific aspects were calculated. The correlations in order from strongest to weakest were treatment burden ($r(156) = .26$, $p < .001$), life expectancy ($r(156) = .16$, $p < .05$), psychological & emotional health ($r(156) = .13$, $p < .05$), social functioning & personal goal fulfillment ($r(156) = .13$, $p < .05$), and physical health ($r(156) = .07$, not significant).

Table 1 Estimate the overall impact that CF will have on each aspect of the affected individual's life. (F508del homozygote)

	Little to no impact (1)	Some impact (2)	Significant impact (3)	Profound impact (4)	Mean $n = 157$	S.D.
Physical health	0 %	4.5 %	52.2 %	43.3 %	3.39	0.573
Psychological & emotional health	1.9 %	43.9 %	44.6 %	9.6 %	2.62	0.684
Social functioning & personal goal fulfillment	5.1 %	66.2 %	23.6 %	5.1 %	2.29	0.641
Treatment burden	0 %	13.4 %	65 %	21.7 %	3.08	0.588
Life expectancy	0 %	14.6 %	63.1 %	22.3 %	3.08	0.605

Prior Knowledge of an Approved Targeted Treatment

Prior to an informational segment, participants were asked if they had heard of the drug ivacaftor (Kalydeco™). While the survey specified the brand and generic names to gauge awareness and familiarity with the approved treatment, we are referring to this treatment as "the drug" or its generic identifier, ivacaftor, for the purposes of this paper. Eighty-nine respondents (58.2 %) had 'never heard of it.' Thirty- three respondents (21.6 %) reported that they had 'heard of it', but were 'not sure exactly' what it was. Twenty-seven respondents (17.6 %) reported they knew 'a little bit about it.' Only four individuals (2.6 %) responded that they knew 'quite a bit' about the drug.

Perception & Discussion of the Targeted Treatment

After reading an informational segment about the drug, participants estimated the overall impact that ivacaftor might have on an affected individual's life. Ratings indicated that the drug was estimated to have between 'some' and 'significant' impact in all areas (Table 3). They also rated the likelihood of their discussing this impact and sharing information about the drug with a patient whose fetus is affected with one F508del CFTR mutation and one G551D CFTR mutation. The results indicated that the counselors would 'probably' discuss the impact of the targeted treatment in all areas (Table 4). Respondents were asked what they might discuss about the drug in a follow-up to discuss the result. The majority (74.5 %) would 'definitely' discuss a referral to a specialist (M = 3.68), and 'probably' discuss clinical trial results (M = 3.34) Respondents were less likely to discuss anecdotes about patient experiences with the drug (M = 2.46) (Table 5).

A counselor's estimate regarding the likely effect of ivacaftor was correlated with an increased likelihood of discussion in all five areas of impact. From strongest to weakest, the correlations were: life expectancy ($r(146) = .37$, $p < .001$); social functioning & personal goal fulfillment ($r(146) = .34$, $p < .001$); treatment burden ($r(146) = .31$, $p < .001$); physical health ($r(146) = .31$, $p < .001$); psychological & emotional health ($r(146) = .23$, $p < .01$).

Respondents were asked to rate their level of agreement with a list of statements regarding ivacaftor. The results are shown in Table 6. In general, the genetic counselors were agreed that they were concerned that there is not enough data to support the benefits of the treatment, that by discussing it they might be instilling false hope, that information about this targeted therapy would be best explained by a specialist, that the drug is too costly, and that there is no long term data available. They also disagreed that information about the drug would not affect a patient's decision to continue or terminate the pregnancy.

Perception and Discussion of Treatments Pending FDA-approval

Ivacaftor alone is not effective for patients homozygous for F508del mutations (Clancy et al. 2011), the genotype present in the approximately 50 % of patients with CF in the United States (CFF, Cystic Fibrosis Foundation 2014). However, a second type of modulation therapy, known as a corrector, is in clinical trials as a potential treatment in combination with

Table 2 The patient and her partner return for a follow up appointment to discuss the result. At this time, would you address the impact of CF on the following aspects of the affected individual's life? (F508del homozygote)

	Definitely not (1)	Probably not (2)	Probably (3)	Definitely (4)	Mean $n = 154$	S.D.
Physical health	0 %	0 %	5.8 %	94.2 %	3.94	0.235
Psychological & emotional health	1.3 %	25.3 %	50.6 %	22.7 %	2.95	0.730
Social functioning & personal goal fulfillment	1.3 %	29.9 %	44.8 %	24 %	2.92	0.767
Treatment burden	0.6 %	4.5 %	24 %	70.8 %	3.65	0.600
Life expectancy	0 %	0 %	13.6 %	86.4 %	3.86	0.344

Table 3 Estimate the overall impact that (the drug) may have on an each aspect of the affected individual's life. (Question 7) (F508del /G551D compound het)

	Little to no impact (1)	Some impact (2)	Significant impact (3)	Profound impact (4)	Mean $n = 149$	SD
Physical health	0 %	40.9 %	47.7 %	11.4 %	2.70	0.663
Psychological & emotional health	0.7 %	44.3 %	45 %	10.1 %	2.64	0.669
Social functioning & personal goal fulfillment	2.7 %	49.7 %	38.3 %	9.4 %	2.54	0.702
Treatment burden	12.1 %	41.6 %	38.3 %	8.1 %	2.42	0.807
Life expectancy	3.4 %	57 %	32.2 %	7.4 %	2.44	0.681

ivacaftor for patients with F508del mutations (Boyle et al. 2014). With over 2000 CFTR mutations identified, and only a fraction characterized (Sosnay et al. 2013), many mutations will never be studied for specific response to ivacaftor, and decisions regarding its use will be left to clinicians and in some cases, payors.

Participants reviewed a brief informational segment about clinical trials in which ivacaftor is being studied in combination with another drug for treatment of patients with who have two copies of the F508del mutation. There was more ambivalence in how to counsel patients about treatments pending FDA approval. Approximately 45 % of respondents stated they would discuss unapproved treatments in the pipeline with a patient whose fetus is affected with two F508del mutations. Approximately 54 % of respondents stated they would not discuss unapproved treatments with a patient in this scenario.

Respondents rated their level of agreement with a list of statements pertaining to unapproved treatments. The results are shown in Table 7. In general, the counselors agreed that there is not enough data to support the benefits of potential treatments and that they would be concerned that by discussing treatments pending FDA approval, they may instill false hope. Approximately 39.7 % of counselors 'disagreed' or 'strongly disagreed' that information about potential treatments would not affect a decision to terminate a pregnancy.

Discussion

An essential role of the genetic counselor is to provide information about genetic conditions, including education about management, prevention, resources and research, and counseling to promote informed choices and adaptation to the risk or condition. (National Society of Genetic Counselors' Definition Task Force 2006). In the prenatal setting, information provided during the counseling sessions may set expectations for management of the disease trajectory, which in turn may influence the prospective parents' decision to continue or terminate a pregnancy after receiving a fetal diagnosis. Ioannou et al. (2015) described the experiences of ten Australian couples at 1 in 4 risk to have a child with CF, all of whom changed their reproductive behavior as a result of their carrier status, including two who terminated affected pregnancies. The current survey results indicate that there are many factors which influence counselor's views toward sharing information about new treatment options in the prenatal genetic counseling arena both generally, and with regard to a prenatal diagnosis of CF. The response to the survey suggests that these attitudes are shaped by counselors' level of familiarity with the treatment and their perception of its benefits and limitations, their comfort level discussing these subjects, and their interpretation of the genetic counselor's role and that of the CF specialist.

The survey elicited a range of responses in regard to respondents' views on the potential for a targeted treatment to impact an affected individual's physical health, psychological & emotional health, social functioning & personal goal fulfillment, treatment burden, and life expectancy. In each case, after reviewing information about the drug, 40–60 % of counselors felt it would have 'little to no' or 'some' impact, while the remaining 40–60 % felt it would have a 'significant' or 'profound' impact. Counselors' perceptions of ivacaftor the

Table 4 Would you address the possibility for (the drug) to impact the following aspects of the affected individual's life? (Question 9) (F508del /G551D compound het)

	Definitely not (1)	Probably not (2)	Probably (3)	Definitely (4)	Mean $n = 147$	SD
Physical health	1.4 %	8.2 %	54.4 %	36.1 %	3.25	0.660
Psychological & emotional health	2.7 %	34.7 %	47.6 %	15 %	2.75	0.739
Social functioning & personal goal fulfillment	2.7 %	33.3 %	48.3 %	15.6 %	2.77	0.741
Treatment burden	2.7 %	19.7 %	46.9 %	30.6 %	3.05	0.783
Life expectancy	4.8 %	29.3 %	42.2 %	23.8 %	2.85	0.839

Table 5 You schedule a follow-up appointment with the patient and her partner to discuss the result. Regarding (the drug), you would choose to share the following with this patient. (Question 8) (F508del /G551D compound het)

	Definitely not (1)	Probably not (2)	Probably (3)	Definitely (4)	Mean $n = 154$
Name of the drug	1.4 %	17.1 %	37 %	44.5 %	3.25
Summary of clinical trial results	1.4 %	6.8 %	48.3 %	43.5 %	3.34
Anecdotes about patient experiences with the drug	11.7 %	40.7 %	37.2 %	10.3 %	2.46
Referral to a specialist	1.3 %	4 %	20.1 %	74.5 %	3.68

treatment varied much more than their perceptions of the impact of CF in general. Potential benefits of the drug that were viewed as more significant were more likely to be discussed by counselors, and vice versa. The correlations between the counselors' perceptions of the drug's benefits and their likelihood of being discussed were much stronger than those found between each counselor's perception of the impact of CF on various aspects of physical or emotional functioning and their likelihood of being discussed. This finding suggests that information about a targeted treatment may have a greater impact on what the counselor chooses to discuss than information on CF in general. It also suggests that a counselor's perception of what treatment options are available and how well they work may be an important factor driving the conversation between counselor and prospective parents in a prenatal setting.

The introduction of genetic modulation therapies is a significant advancement in treating CF and has the potential to impact an affected individual's health-related quality of life. Individuals taking the medication may perceive the overall burden of CF differently than if they were using traditional treatment modalities. Physical health, psychological & emotional health, social functioning & personal goal fulfillment, treatment burden, and life expectancy are areas which may be positively impacted. However, the extent to which patients will benefit cannot yet be clearly defined. While media reports suggest a positive impact, quality of life improvements have been documented only with respect to respiratory symptoms (Ramsey et al. 2011). Additionally, the drug has only been approved for genotypes that encompass a minority of patients, making this exciting development an option for only 4–5 % of patients with CF (CFF, Cystic Fibrosis Foundation 2014).

The possibility for quality of life improvements for patients taking targeted therapies, combined with our current inability to precisely quantify these benefits make it difficult to determine how this potential should be presented to a patient whose fetus is affected with CF. This uncertainty likely contributes to differences among respondents regarding how to counsel. Measuring improvements with respect to physical health, psychological & emotional health, social functioning & personal goal fulfillment, treatment burden, and life expectancy would be useful for counselors but is associated with various challenges.

Counselors were less likely to discuss the potential impact of the targeted therapy with respect to social functioning & personal goal fulfillment and psychological & emotional health than physical health, treatment burden, and life expectancy, and accordingly they are less likely to bring these subjective topics into any discussion of CF. Still, counselors' disinclination to discuss social functioning & personal goal fulfillment and psychological health & emotional health was in keeping with their ranking of these aspects of functioning overall, which they described as the least impacted by CF. On the other hand, counselors ranked social functioning & personal goal fulfillment and psychological & emotional health second and third among those aspects of life that would be impacted by this treatment, just behind life

Table 6 To what extent do you agree or disagree with the following statements? (Question 10)

	Strongly disagree (1)	Disagree (2)	Neither agree or disagree (3)	Agree (4)	Strongly agree (5)	Mean $n = 147$
I am concerned that there is not enough data to support the benefits of this drug.[a]	0 %	15.7 %	27.9 %	53.7 %	2.7 %	3.44
I would be concerned that by discussing this drug with patients, I may instill false hope.	1.4 %	15.7 %	19.1 %	54.4 %	9.5 %	3.55
I feel that info about this drug would be best explained by a specialist.	0 %	8.2 %	10.3 %	42.5 %	39 %	4.12
I feel that info about this drug would not likely affect a patient's decision to continue or terminate the pregnancy.	6.8 %	41.5 %	30.7 %	17.7 %	3.4 %	2.69
The cost of this drug is concerning.	0 %	0.7 %	6.1 %	38.8 %	54.4 %	4.47
It is concerning that this drug is not approved for children under 6.	0.7 %	19.7 %	33.3 %	36.7 %	9.5 %	3.35
It is concerning that no long term data for this drug is currently available.	0.7 %	2.0 %	8.2 %	55.8 %	33.3 %	4.19

[a] In the survey, "drug" referred specifically to ivacaftor (Kalydeco™)

Table 7 To what extent do you agree or disagree with the following statements? (Question 12)

	Strongly disagree (1)	Disagree (2)	Neither agree or disagree (3)	Agree (4)	Strongly agree (5)	Mean $n = 147$
I am concerned that there is not enough data to support the benefits of potential treatments.	0 %	4.1 %	15.2 %	51.7 %	29.0 %	4.06
I would be concerned that by discussing treatments pending FDA- approval, I may instill false hope.	0.7 %	10.3 %	12.4 %	51.0 %	25.5 %	3.9
I feel that info about treatments pending FDA-approval would be best explained by a specialist.	0 %	10.3 %	11.0 %	45.2 %	33.6 %	4.02
I feel that info about treatments pending FDA-approval would not likely affect a patient's decision to continue or terminate the pregnancy.	2.7 %	37.0 %	26.7 %	25.3 %	8.2 %	2.99

expectancy and treatment burden, but this did not make them more likely to include them in their prenatal discussions. Our results indicate that while treatment burden would be discussed in a results session if a counselor perceived its impact as substantial, physical health would be discussed regardless of the counselor's perception of impact.

A continuing problem that likely affects counseling strategy is that improvement in subjective areas has not been validated by concrete data. One respondent commented, "the reason I would not discuss a lot of the psychological and social health aspects is because there is no research yet that shows the drug improves psychological health and social functioning." Patient successes portrayed in the media, which focus on psychosocial and emotional improvement, may influence a counselor's belief that the drug will positively influence some patients. It might appear evident that improvements in physical health would have implications for emotional health and functioning. However, the absence of metrics which demonstrate the drug's ability to impact psychological well-being could make counselors hesitate to raise the issues.

But absence of longitudinal data also makes it difficult to predict any impact on life expectancy. Ivacaftor has been shown to reduce the number of pulmonary exacerbations, a contributor to irreversible lung damage in patients with CF. It has been inferred that long term use of this treatment will slow lung disease progression and therefore lengthen life span. However, since the treatment is new this benefit can only be hypothetical. Nonetheless, approximately two-thirds of counselors said they would 'definitely' or 'probably' discuss with patients the possible impact of ivacaftor on life expectancy. This suggests that absence of data may not create as much discomfort as subjectivity.

Counselors were most strongly in agreement about the drug's potential impact on physical health, which is both a less subjective topic and the best supported in terms of current data, which shows improvements in measurements of lung function, number of pulmonary exacerbations, and weight gain. Physical health improvements were perceived by counselors as the greatest benefit of the drug and the most likely to be discussed. Likewise, physical health was also most likely to be discussed by counselors in their general discussion of CF.

Over 90 % of counselors indicated they would be likely to share some level of information with prospective parents about the potential impacts of this treatment on their affected child, if the genotype of the fetus was such that this targeted treatment was an already approved option for this individual, Almost all counselors (95 %) surveyed would refer patients to a specialist to discuss the drug in this scenario. However, the majority of all participants (80 %) initially reported that they had never heard of ivacaftor or they were not sure exactly what it was. About 18 % of counselors said they knew a little bit about it and a small fraction (2.6 %) of counselors said they knew quite a bit about it. This suggests a gap between the knowledge of counselors with regard to targeted treatments for CF and the information they feel is appropriate to impart to their patients who have a received a prenatal diagnosis of CF, if the genotype is such that there is an approved genetic modulation therapy.

Many responses suggested that the counselors themselves did not feel prepared to discuss targeted treatments, even those that are FDA-approved. Counselors were largely in agreement that the targeted treatment should be presented to prospective parents of a fetus with a prenatal diagnosis of CF, but they had varying ideas about the content and level of discussion which they felt comfortable sharing in a genetic counseling session. Most participants (80 %) indicated that information about the treatment would be best explained by a specialist. However, if counselors do not discuss the potential for available targeted treatments in the reproductive genetics setting, patients may make their pregnancy management decisions without contacting the CF specialist.

Although they may perceive a need for specialists, genetic counselors are likely to introduce the subject of targeted treatments to prospective parents facing a prenatal diagnosis of CF. Regardless of what the counselor perceives to be the appropriate depth for this conversation in the context of a genetic counseling session, there is a need for counselors to incorporate discussion of new treatment options into their counseling. Educating genetic counselors about new targeted treatments for CF may be accomplished through sessions at an upcoming National Society of Genetic Counselors (NSGC) conference, the development of educational tools, and the establishment of practice guidelines which could further define the roles of a genetic

counselor in these scenarios. The genetic counseling community may wish to consider more carefully the respective responsibilities of the counselor and the specialist in the prenatal setting.

Those providing resources should consider carefully how to address areas where we have limited data, such as life expectancy and psychological impact, and how these may be discussed. Suggestions for managing expectations of prospective parents would be beneficial to counselors since approximately 65 % of counselors stated they were concerned that by discussing the drug, they may instill false hope in their patients. One counselor commented, "I think that couples that are properly counseled would understand that there are no guarantees with the drug for improvement, thus minimizing false hopes. If couples aren't properly counseled, I'd be concerned that info about ivacaftor may make some couples overly hopeful. Proper counseling (whether by a genetic counselor or specialist administering treatment) is critical."

Whereas almost every counselor surveyed felt that the availability of ivacaftor should be presented to prospective parents whose fetus is affected with at least one G551D mutation, there was no consensus on how to proceed when a fetus has only F508del mutations. In this situation, a little more than half of all counselors (54.4 %) said they would 'probably not' or 'definitely not' discuss potential future treatments. One counselor stated, "unapproved treatments are just that and should not be part of the discussion about treatment. Patients need information about what we can do today, not what we may or may not be able to do tomorrow." On the other hand, 44.6 % would discuss treatments in the pipeline, and as another counselor stated, "I feel it would be negligent not to mention target drugs are being developed for certain mutations." It is impossible to be certain when or if treatments in the pipeline will reach the market, and what their efficacy might be, however, by withholding information about potential treatment options, counselors may be depicting CF in a way which is inaccurate for children born with the condition in this era.

Potentially the greatest limitation of the treatments is one of access. Almost all respondents (93.3 %) either agreed or strongly agreed that they were concerned about the cost of the medication. Though we did not specifically explore it in the present study, genetic counselors may be concerned about discussing an expensive drug and access issues should be covered in any educational effort or resource.

Limitations & Future Directions

This project had several limitations. The study has limited generalizability and is based on a response rate of only 24 % from the NSGC list of over 800 prenatal counselors. The survey tool used for this study was not validated, and did not assess basic knowledge of genetics. Baker et al. (2013) have previously reported that genetic counselors scored highly on a basic knowledge questionnaire about the genetics of cystic fibrosis. The CFQ-R domains were used in the development of this project's survey since they encompass many factors which may help to assess the quality of life of someone with CF; hence they are helpful in presenting information about how CF may impact a person's life. Individuals who utilize prenatal diagnosis for CF may wish to prepare for the birth of a child with CF or prevent the birth of a child with CF. When disclosing a prenatal diagnosis, one of the main goals of the prenatal genetic counselor is to educate the patient about the consequences of that disease in a balanced and complete manner. While this study did not examine respondents' knowledge of genetics, the information gleaned from this survey provides some preliminary insights as to how prenatal genetic counselors evaluate emergent treatment information before incorporating it into discussions with expectant parents

Studies are needed to determine whether information about genotype-specific treatments, both approved and those pending approval, will affect patient's decisions to continue or terminate a pregnancy affected with CF. This information would offer insight into the relevance and impact of introducing these topics at the time of a prenatal diagnosis. CF specialist's responses to these questions could also serve as a basis of comparison.

Conclusion

A majority of counselors surveyed believe that discussion of targeted treatments for CF is an appropriate subject following a prenatal diagnosis of CF, in those cases when a treatment is currently available for individuals with the genotype of the fetus. For the more common F508del mutation, with no genetic modulation treatment on the market at the time of the survey, there was not consensus about the appropriateness of discussing potential breakthroughs. Counseling patients about targeted treatments for CF may become more relevant as targeted treatments, effective for patients with more common CF genotypes, are being brought to market, including combination therapy for F508del homozygotes age 12 and older. This will likely present educational challenges for genetic counselors and spark questions about the genetic counselor's role. As more personalized medicine options become available, the issues which have been raised in this project are likely to become applicable for other genotypes as well as for other genetic conditions. Finding an effective way to educate prenatal genetic counselors about currently approved genetic modulation therapies may serve as a model for other targeted treatments as they become available.

Compliance with Ethical Standards

Conflict of Interest None of the authors have any personal affiliation or financial interest in Vertex Pharmaceuticals, manufacturer of ivacaftor, or in any other manufacturer of cystic fibrosis treatments.

Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

Animal Studies No animal studies were carried out by the authors for this article.

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