

Characterization and Waiting List Outcomes of Patients With Cystic Fibrosis Listed for Lung Transplantation

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INTRODUCTION

- Cystic fibrosis (CF) is the third most common indication for lung transplantation¹ and is often the only remaining option for patients with CF who have end-stage lung disease²
- While prior studies³⁻⁷ have evaluated post-transplantation outcomes, patients with CF who are waiting for a lung transplant have not been well characterized

OBJECTIVES

- To characterize patients with CF at the time of listing on the lung transplant waiting list and describe their outcomes while on the waiting list
- To characterize the subset of those patients who received a lung transplant

METHODS

- This retrospective cohort study used data from the Scientific Registry of Transplant Recipients (SRTR) Standard Analytic File⁸ for 2006-2014
 - The year 2006 was chosen as the first full calendar year during which the lung allocation score was implemented, and 2014 was the last calendar year for which data were available at the time this analysis was undertaken
 - The SRTR includes data on all organ donors, waiting list candidates, and transplant recipients in the United States
 - This study included only candidates and recipients whose lung transplant candidate registration form indicated a primary diagnosis of CF

Characterization of the Overall Lung Transplant Waiting List for Patients With CF (2006-2014)

- To characterize the overall lung transplant waiting list for patients with CF, the waiting list was examined for each calendar year between 2006 and 2014. For each year, the number of patients was summarized who were
 - On the waiting list as of January 1 of the relevant year
 - Listed for lung transplantation during the relevant year, including patients who had a previous lung transplant or previous listing
- Patients were only counted once per year but could be included in multiple years
- Among all patients included within a given year (those on the waiting list as of January 1 and those listed during the year), the waiting list outcome recorded within that year for each patient was summarized. The outcomes were: 1) received lung transplant; 2) did not survive; or 3) removed from list for other reasons. Patients who remained on the list as of December 31 of that year were categorized as still waiting

Candidate and Waiting List Outcomes Analyses Among Newly Listed Patients

- The cohort used for these analyses (the "candidate cohort") included patients with CF who were added to the waiting list during 2006-2012, had no record of previous lung or heart-lung transplant, and had no previous listing for a lung transplant
- Candidate Demographics and Clinical Characteristics Analysis
 - Demographic and clinical characteristics for the candidate cohort were summarized overall and stratified by age at listing (12-17 vs ≥18)
 - Functional status was reported using the Karnofsky performance score for adult patients and the Lansky performance score for pediatric patients. This metric is reported in 10% increments between 10% and 100%
 - Patients were grouped into 3 categories of functional status restrictions as defined by their Karnofsky or Lansky performance score as appropriate. The 3 categories were (1) severe to moderate restriction (10%-40%), (2) moderate to mild restriction (50%-70%), and (3) normal activity (80%-100%)
- Counts and percentages were used for categorical variables, and mean (± standard deviation [SD]) and median (with interquartile range [IQR]) were used for continuous variables

Waiting List Outcomes Analyses

- Patients from the candidate cohort were followed from listing date until the earliest of removal from the waiting list (any reason) or the date 2 years after listing. Outcomes were collected 1, 3, 6, 12, and 24 months post listing
- Five outcome measures were used to classify patients: 1) received lung transplant; 2) did not survive; 3) improved health so lung transplant not needed; 4) became ineligible for transplant due to disease progression; or 5) other
- Results were summarized overall and stratified by age at listing (12-17 vs ≥18). The results for adults were also stratified by primary source of payment (public or private)

Recipient Analyses

- The cohort used for these analyses (the "recipient cohort") included the subset of patients from the candidate cohort whose listing ended in a lung transplant before January 1, 2015
- Demographic and clinical characteristics for the recipient cohort were summarized using the methods described above for the candidate cohort, except that age at time of transplant was used in place of age at listing
- Patients in the recipient cohort were also categorized based on the time elapsing between their listing date and the date of transplantation: <1, 1 to <3, 3 to <6, 6 to <12, and ≥12 months

RESULTS

Summary of the Overall Lung Transplant Waiting List for Patients With CF (2006-2014)

- From 2006-2012, the annual number of patients with CF who were on the lung transplant waiting list as of January 1 of each year appeared to decline, then remained stable through 2014
- The number of patients who received a lung transplant appeared to remain relatively stable between 2006 and 2014 (range: 179-243) (Table 1)

| Table 1. Characterization of the Overall Lung Transplant Waiting List for Patients With CF (2006-2014) | | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|--|--|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Patients on waiting list on January 1 | | 460 | 418 | 325 | 264 | 237 | 225 | 181 | 182 | 184 |
| Patients listed during the year | | 235 | 216 | 202 | 289 | 288 | 260 | 267 | 297 | 268 |
| Outcomes before end of the year, n (%) | | | | | | | | | | |
| Received transplant | | 216 (31.1) | 193 (30.4) | 179 (34.0) | 228 (41.2) | 210 (40.0) | 243 (50.1) | 202 (45.1) | 238 (49.7) | 215 (47.6) |
| Did not survive | | 32 (4.6) | 48 (7.6) | 41 (7.8) | 35 (6.3) | 38 (7.2) | 19 (3.9) | 25 (5.6) | 19 (4.0) | 27 (6.0) |
| Removed from list/other | | 37 (5.3) | 77 (12.1) | 41 (7.8) | 55 (9.9) | 58 (11.0) | 43 (8.9) | 41 (9.2) | 42 (8.8) | 39 (8.6) |
| Still waiting | | 410 (59.0) | 316 (49.8) | 266 (50.5) | 235 (42.5) | 219 (41.7) | 180 (37.1) | 180 (40.2) | 180 (37.6) | 171 (37.8) |

CF, cystic fibrosis.

Candidate and Waiting List Outcomes Analyses Among Newly Listed Patients

Candidate Analyses

- There were 1781 new candidates for lung transplantation with CF from 2006-2012. Demographic and clinical characteristics at the time of listing for these patients are shown in Table 2

Table 2. Demographic and Clinical Characteristics at the Time of Listing for All Patients in the Candidate Cohort: All Patients With CF Added to the Lung Transplantation Waiting List During 2006-2012*

| Characteristic | Age 12-17 Years | Age ≥18 Years | Overall [†] |
|---|-------------------|-------------------|----------------------|
| Total patients | 198 | 1533 | 1781 |
| Age at listing, median (IQR) | 15.0 (14.0, 16.0) | 28.0 (23.0, 36.0) | 26.0 (21.0, 34.0) |
| Female, n (%) | 131 (66.2) | 750 (48.9) | 905 (50.8) |
| BMI at listing, mean (SD) | 17.6 (2.3) | 19.6 (2.9) | 19.2 (2.9) |
| BMI group, n (%) | | | |
| <17 | 68 (34.3) | 153 (10.0) | 255 (14.3) |
| 17 to <20 | 92 (46.5) | 709 (46.2) | 814 (45.7) |
| 20 to <22 | 24 (12.1) | 367 (23.9) | 394 (22.1) |
| ≥22 | 14 (7.1) | 304 (19.8) | 318 (17.9) |
| Primary source of payment, n (%) | | | |
| Private insurance | 101 (51.0) | 888 (57.9) | 1011 (56.8) |
| Public insurance | 94 (47.5) | 637 (41.6) | 756 (42.4) |
| Diabetes, n (%) | | | |
| Yes | 81 (40.9) | 716 (46.7) | 812 (45.6) |
| No | 117 (59.1) | 802 (52.3) | 954 (53.6) |
| IV-treated pulmonary sepsis episodes (≥2) in last year, n (%) | | | |
| Yes | 119 (60.1) | 608 (39.7) | 752 (42.2) |
| No | 56 (28.3) | 670 (43.7) | 745 (41.8) |
| Pan-resistant bacterial lung infection, n (%) | | | |
| Yes | 53 (26.8) | 296 (19.3) | 360 (20.2) |
| No | 134 (67.7) | 1148 (74.9) | 1319 (74.1) |
| ppFEV ₁ at listing, median (IQR) | 26.0 (21.0, 33.0) | 23.0 (19.0, 28.0) | 23.0 (19.0, 28.0) |
| ppFEV ₁ at listing, n (%) | | | |
| <20 | 32 (16.2) | 404 (26.4) | 442 (24.8) |
| 20 to <30 | 82 (41.4) | 731 (47.7) | 822 (46.2) |
| 30 to <40 | 49 (24.8) | 204 (13.3) | 268 (15.0) |
| 40+ | 22 (11.1) | 43 (2.8) | 80 (4.5) |
| Life support (all categories), [‡] n (%) | 11 (5.6) | 118 (7.7) | 132 (7.4) |
| Functional status category, n (%) | | | |
| Severe to moderate restriction (10%-40%) | 33 (16.7) | 372 (24.3) | 409 (23.0) |
| Moderate to mild restriction (50%-70%) | 111 (56.1) | 918 (59.9) | 1059 (59.5) |
| Normal activity (80%-100%) | 49 (24.7) | 231 (15.1) | 295 (16.6) |
| Unknown/NA | 5 (2.5) | 12 (0.8) | 18 (1.0) |

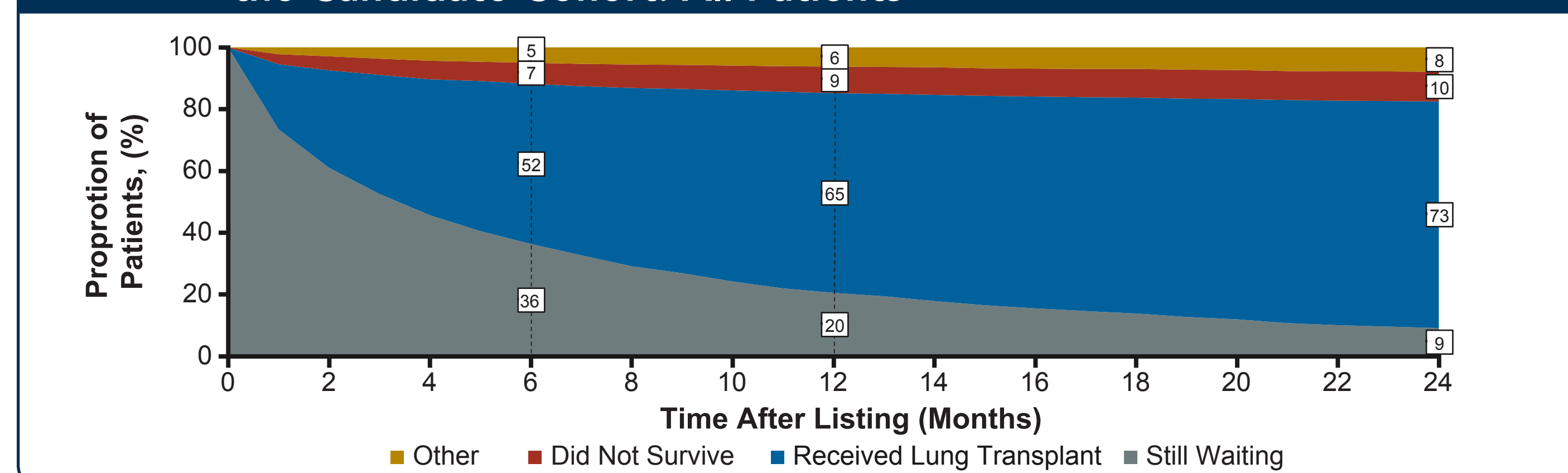
* Some categories may not sum to the column total due to missing or unknown data for some patients. [†] Of the 1781 candidates, ages at listing were 0-5, 5 (0.3%); 6-11, 45 (2.5%); 12-17, 198 (11.1%); and ≥18, 1533 (86.1%). [‡] Life support categories: extracorporeal membrane O₂ (ECMO), no ventilator; ventilator, no ECMO; both ECMO and ventilator; other life support. BMI, body mass index; IQR, interquartile range; IV, intravenous; NA, not applicable; ppFEV₁, percent predicted forced expiratory volume in 1 second; SD, standard deviation.

- Overall, 3% of candidates were aged ≤11 years at listing, 11% were aged 12-17, and 86% were aged ≥18
- Nearly a quarter of patients had moderate to severe functional restrictions (Table 2)
- Compared to candidates aged ≥18 years at listing, candidates aged 12-17 years at listing were more likely to have percent predicted forced expiratory volume in 1 second (ppFEV₁) ≥30 (36% vs 16%); additionally, a greater proportion were female (66% vs 49%), had a functional status score in the normal activity range (25% vs 15%), and had ≥2 intravenous (IV)-treated pulmonary sepsis episodes in the year before listing (60% vs 40%) (Table 2)

Waiting List Outcomes Analyses: Overall

- Most candidates (91%) were removed from the waiting list within 24 months, including 73% who received a lung transplant, 10% who did not survive (Figure 1), and 5% who became ineligible due to disease progression
 - 1% of patients were removed from the list due to improved health
 - After 24 months, 9% were still waiting to receive a lung transplant (Figure 1)

Figure 1. Waiting List Outcomes in the 24 Months Postlisting for Patients in the Candidate Cohort: All Patients



- The median time to lung transplantation was 3 months (IQR: 1-7) among those who received a lung transplant
- While 21% of waiting list candidates received a lung transplant within 1 month of listing, many waited longer; of those receiving a lung transplant within 24 months, 29% waited >6 months

Waiting List Outcomes Analyses: Subgroups

- A smaller percentage of patients aged 12-17 years at time of listing received a lung transplant within 24 months (Table 3) compared with patients aged ≥18 years (Table 4) (65% vs 75%, respectively)

Table 3. Waiting List Outcomes in the 24 Months After Listing for Patients in the Candidate Cohort Aged 12-17 at Time of Listing

| Outcome | Months Since Listing | | | | | Within 24 Months | |
|--|----------------------|----------------|----------------|-----------------|--------------------------------|------------------|--|
| | 1 Month n (%) | 3 Months n (%) | 6 Months n (%) | 12 Months n (%) | Months to Outcome Median (IQR) | n (%) | |
| Transplant | 31 (15.7) | 62 (31.3) | 84 (42.4) | 112 (56.6) | 4 (1, 8) | 129 (65.2) | |
| Did not survive | 10 (5.1) | 16 (8.1) | 19 (9.6) | 21 (10.6) | 2 (0, 12) | 27 (13.6) | |
| Improved health, transplant not needed | 0 | 1 (0.5) | 1 (0.5) | 1 (0.5) | 3 (3, 3) | 1 (0.5) | |
| Ineligible due to disease progression | 2 (1.0) | 4 (2.0) | 6 (3.0) | 7 (3.5) | 3 (1, 7) | 8 (4.0) | |
| Other | 0 | 0 | 1 (0.5) | 3 (1.5) | 10 (9, 13) | 5 (2.5) | |
| Still waiting | 155 (78.3) | 115 (58.1) | 87 (43.9) | 54 (27.3) | NA | 28 (14.1) | |

IQR, interquartile range; NA, not applicable.

Table 4. Waiting List Outcomes in the 24 Months After Listing for Patients in the Candidate Cohort Aged ≥18 at Time of Listing

| Outcome | Months Since Listing | | | | Within 24 Months | |
|--|----------------------|----------------|----------------|-----------------|--------------------------------|-------------|
| | 1 Month n (%) | 3 Months n (%) | 6 Months n (%) | 12 Months n (%) | Months to Outcome Median (IQR) | n (%) |
| Transplant | 335 (21.9) | 612 (39.9) | 824 (53.8) | 1017 (66.3) | 3 (1, 7) | 1150 (75.0) |
| Did not survive | 44 (2.9) | 74 (4.8) | 99 (6.5) | 122 (8.0) | 3 (1, 6) | 133 (8.7) |
| Improved health, transplant not needed | 1 (0.1) | 3 (0.2) | 4 (0.3) | 9 (0.6) | 8 (3, 19) | 15 (1.0) |
| Ineligible due to disease progression | 31 (2.0) | 46 (3.0) | 62 (4.0) | 66 (4.3) | 2 (1, 5) | 76 (5.0) |
| Other | 4 (0.3) | 8 (0.5) | 12 (0.8) | 21 (1.4) | 9 (3, 13) | 29 (1.9) |
| Still waiting | 1118 (72.9) | 790 (51.5) | 532 (34.7) | 298 (19.4) | NA | 130 (8.5) |

IQR, interquartile range; NA, not applicable.

- 25% of adult patients whose primary payment source was private insurance received a lung transplant within 1 month of listing, compared with 17% of those with public insurance

Recipient Analyses

- The characteristics of the 1393 candidates who received a lung transplant before January 1, 2015 are shown in Table 5. Age, sex, and source of payment were similar to those of the overall waiting list candidate cohort (Table 2)

Table 5. Select Demographic and Clinical Characteristics at Time of Lung Transplant for Patients With CF in the Recipient Cohort: All Patients in the Candidate Cohort Who Received a Lung Transplant During 2006 to 2014*

| Characteristic | Age 12-17 Years | Age ≥18 Years | Overall [†] |
|--------------------------------------|-------------------|-------------------|----------------------|
| Overall, n (%) | 130 (100.0) | 1239 (100.0) | 1393 (100.0) |
| Age at transplant, median (IQR) | 16.0 (14.0, 17.0) | 29.0 (24.0, 37.0) | 28.0 (22.0, 36.0) |
| Female, n (%) | 84 (64.6) | 576 (46.5) | 670 (48.1) |
| Time to transplantation group, n (%) | | | |
| <1 month | 31 (23.8) | 335 (27.0) | 370 (26.6) |
| 1 to <3 months | 31 (23.8) | 277 (22.4) | 313 (22.5) |
| 3 to <6 months | 22 (16.9) | 213 (17.2) | 241 (17.3) |
| 6 to <12 months | 25 (19.2) | 196 (15.8) | 228 (16.4) |
| ≥12 months | 21 (16.2) | 218 (17.6) | 241 (17.3) |
| Primary source of payment, n (%) | | | |
| Private insurance | 65 (50.0) | 714 (57.6) | 791 (56.8) |
| Public insurance | 63 (48.5) | 520 (42.0) | 593 (42.6) |

* Some categories may not sum to the column total due to missing or unknown data for some patients. [†] Of the 1393 candidates, ages at transplant were 0-5, 1 (0.1%); 6-11, 23 (1.7%); 12-17, 130 (9.3%); and ≥18, 1239 (88.9%). IQR, interquartile range.

- Overall, 17% of recipients waited 12 months or more before receiving a lung transplant (Table 5)
- Among the recipient cohort, 79 (6%) received an additional lung transplant within the study period; the median (IQR) time to retransplant was 30.6 (18.8, 46.5) months

LIMITATIONS

- This was a retrospective observational study, thus the endpoints included and analyses performed were limited by the nature of the available data. In particular, the SRTR database:
 - Does not include data on patients' CFTR genotype or on patients' disease management therapies, including CFTR modulator therapies
 - Includes limited granularity on patients' insurance type
- Sample size in pediatric patients was limited
- Finally, statistical testing was not performed, limiting interpretation of the comparisons of subgroups within cohorts

CONCLUSIONS

- The disease state among patients with CF on the lung transplant waiting list was severe, as reflected in reduced lung function, functional limitations, presence of comorbidities and complications, and use of life support
- Once listed for lung transplantation, few patients were removed from the list due to improved health
- While many patients received a lung transplant within 24 months, nearly a third waited ≥6 months for a lung transplant, and 10% did not survive
- Given the severity of disease among these patients and the fact that not all may receive a transplant once listed, maintaining health and delaying disease progression is critical in patients with CF

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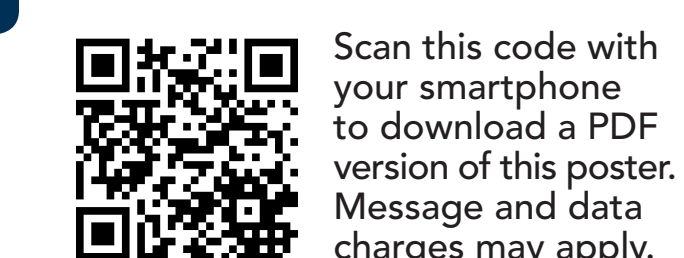
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AUTHOR DISCLOSURES

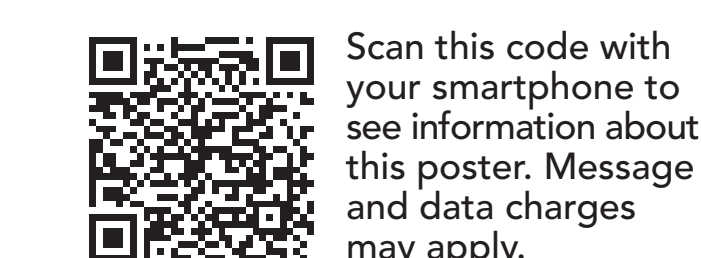
LO, ES, and DW are employees of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company. JM, YP, and JS are employees of Chronic Disease Research Group, which received funding from Vertex Pharmaceuticals Incorporated.

ACKNOWLEDGEMENTS

Editorial coordination and support were provided by Dhruvad Patel, PharmD. DP is an employee of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company. Medical writing and editorial support were provided by Jeremy Kennard, PhD, and Mary Kacilas. JK and MK are employees of Ashfield Healthcare Communications, which received funding from Vertex Pharmaceuticals Incorporated.



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