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RESEARCH ARTICLE

Gilteritinib clinical activity in relapsed/refractory *FLT3* mutated acute myeloid leukemia previously treated with *FLT3* inhibitors

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Abstract

Gilteritinib is approved for the treatment of relapsed/refractory (R/R) acute myeloid leukemia (AML) with an FLT3-mutation (*FLT3*$^{mut+}$). However, the gilteritinib phase 3 ADMIRAL study (Perl et al NEJM 2019) was conducted prior to widespread adoption of either midostaurin as a component of standard intensive induction and consolidation or posttransplant FLT3 inhibitor maintenance. We performed a retrospective analysis using data from 11 US centers and where we identified 113 patients who received gilteritinib alone or as combination therapy for the treatment of R/R *FLT3*$^{mut+}$ AML. The composite complete remission (CR) rate (CRc, defined as CR + CR_i + CR with incomplete platelet recovery [CRp]) was 48.7% ($n = 55$). The CRc rate after treatment with gilteritinib in patients who were treated with only prior 7+3 and midostaurin with or without consolidation was 58% with a median survival of 7.8 months. Survival was longest in patients who obtained a CR, particularly a cMRD

(clinical minimal or measurable residual disease) negative response; this remained significant after censoring at the time of stem cell transplant. The mitogen-activated protein kinase pathway activating mutations that are known for gilteritinib resistance (NRAS, KRAS, and PTPN11) had lower CRc (35% vs. 60.5%) and lower median overall survival than patients' whose leukemia did not express these mutations (4.9 months vs. 7.8 months) (HR 2.4; 95% CI 1. 5.4) *p* value <.01.

1 | INTRODUCTION

Mutations in *FLT3* occur in approximately 30% of patients with new acute myeloid leukemia (AML) and activate intracellular tyrosine kinase signaling to promote cellular proliferation, impair differentiation, and inhibit apoptosis.[1–4]

Historically, FLT3 mutations were associated with early relapse and poor survival with traditional salvage therapy options. Several FLT3 tyrosine kinase inhibitors (FLT3i) have been developed for the treatment of FLT3^{mut} AML.[5,6] The RATIFY (Randomized AML Trial In FLT3 in patients less than 60 years old) trial demonstrated that the addition of midostaurin to induction chemotherapy improved the overall survival and led to the approval of midostaurin in combination with daunorubicin and cytarabine for a new diagnosis of FLT3^{mut} AML.[7] Randomized studies afterward showed a substantial reduction in posttransplant relapse and improved survival from the use of midostaurin and sorafenib as posttransplant maintenance in FLT3-internal tandem duplication (ITD) mutated patients.[8–10]

The ADMIRAL trial was a phase 3 randomized controlled trial that compared the second-generation FLT3i gilteritinib with salvage chemotherapy for the treatment of relapsed or refractory (R/R) FLT3^{mut} AML. A total of 371 patients were randomized 2:1 to either single-agent gilteritinib or their treating physician's prrandomization choice from four standard salvage chemotherapy regimens. The study met its primary endpoint by showing that survival was superior in the gilteritinib arm, with a median overall survival (mOS) of 9.3 months, compared to 5.6 months with chemotherapy (HR 0.64, $p < .001$). However, the ADMIRAL trial enrolled patients prior to widespread use of frontline FLT3is and indeed, only 12.4% of the study population had previously been treated with a FLT3i.[11] Thus, the benefits of gilteritinib in the context of modern therapy incorporating frontline FLT3i's are not well characterized. Additionally, therapy with FLT3i has been shown to drive the expansion of clones with additional on-target mutations, such as FLT3-TKD mutations that may confer resistance to subsequent FLT3i[12] including prior sorafenib therapy.[13] Similarly, other FLT3 mutations, including N676K and F691L, may be associated with resistance to midostaurin or gilteritinib, respectively.[14,15] A more common pattern of resistance to gilteritinib is not on-target mutations in FLT3, but off-target emergent mutations in RAS/mitogen-activated protein kinase (MAPK) pathway genes, including *N-RAS* or *K-RAS*, as well as *PTPN11*. Treatment-emergent mutations in these genes have also been described at progression after frontline intensive chemotherapy with midostaurin.[16] For these reasons, we sought not only to describe the clinical responses but also to clarify whether pretreatment mutations contributed to the response or survival with gilteritinib salvage in patients who have received prior FLT3is and whether such mutations might help inform therapy choice as to single agent versus combination treatment for R/R *FLT3*$^{mut+}$ AML.

2 | METHODS

We performed the largest multi-institutional retrospective analysis from January 2020 to June 2021 in 11 U.S. cancer centers of patients who had received a prior FLT3i and then received gilteritinib alone or as combination therapy for the treatment of R/R *FLT3*$^{mut+}$ AML. Patients were excluded from the analysis if they received gilteritinib: (1) as a part of an ongoing and not reported trial; (2) as a maintenance posttransplant with no documented relapsed disease prior to the start of gilteritinib; (3) because of intolerance to a prior FLT3i due to side effects in a patient in marrow remission; and (4) as frontline therapy with no prior FLT3i exposure. Patient demographic data, as well as disease characteristics, were collected including date of diagnosis, date of relapse date of last follow-up or death, type of treatment at diagnosis and relapse, complete blood counts at diagnosis, the mutational landscape at diagnosis and relapse, and clinical minimal residual disease evaluation. AML risk stratification was assessed based on the 2017 European leukemia net classification.[17]

Response criteria were identical to the ADMIRAL trial, which used a modified version from the international working group response definitions.[18] CR was defined as a morphologic leukemia-free state, a bone marrow regenerating normal hematopoietic cells with a normal marrow differential and <5% blasts, and peripheral blood counts showing an absolute neutrophil count ≥1 $\times$ 10^9/L, platelet count ≥100 $\times$ 10^9/L, transfusion independence for at least 1 week, and no circulating or extramedullary blasts. CR with incomplete platelet recovery (CRp) was defined as CR except for incomplete platelet recovery (<100 $\times$ 10^9/L). CR with incomplete hematological recovery (CRi) was defined as CR except for residual neutropenia <1 $\times$ 10^9/L with or without complete platelet recovery. Transfusion independence was not required for CRi. Composite CR (CRc) was defined as the combined rate of all CR, CRp, and CRi. The investigators from each institution assessed the gilteritinib response on their own patient cohort independently based on the criteria mentioned above. This was done as patient data from each institution was de-identified before it was transferred and combined with the rest of the data set.

Clinical minimal or measurable residual disease (cMRD) was evaluated on bone marrow flow cytometry (MFC) using a cutoff of $<1 \times 10^3$ cells or polymerase chain reaction (PCR) for FLT3 mutation with a minimum sensitivity of 5%. This cMRD assessment was included as the depth of response and was able to be determined at all the centers.

Survival from the time of gilteritinib initiation till death or loss to follow-up was recorded in months. Descriptive statistics were conducted to assess patients' characteristics; *t*-test was performed on continuous variables, and multivariate analysis included all variables collected to determine interaction with patient outcome (response rates and survival in months), and analyses were adjusted for multiple comparisons. Kaplan–Meier curves and log-rank test were used for survival analysis after gilteritinib initiation. A *p*-value of <.05 was considered statically significant. Institutional review board approval and data transfer agreements were obtained from the participating cancer centers.

3 | RESULTS

A total of 410 patients were evaluated from 11 cancer centers and 113 patients were eligible based on the selection criteria. Patient characteristics are shown in Table 1. The median age of the sample was 58.3 years with a range of 18–92 years. About 66 patients were white (58.4%) and 65 were females (57.5%). About 73 patients (64.6%) had a disease that was characterized as favorable or intermediate-risk AML by ELN (four patients had missing next-generation sequencing [NGS] or cytogenetic information). ITD was the most common FLT3 mutation subtype (84.1%) and nine patients (8%) had both mutations (ITD and TKD). The majority of the patients had received midostaurin (57.5%) as a prior FLT3i followed by sorafenib (30%). In this cohort, 49 patients (43.4%) had a history of allogeneic stem-cell transplant (ASCT) prior to receiving gilteritinib and 24 patients (21.2%) underwent ASCT post-gilteritinib therapy. The mean duration of gilteritinib therapy was 4.6 months with a range of 0.2–25 months. The majority of patients received gilteritinib as a single-agent therapy (62.8%) while the remaining patients received gilteritinib in combination with other agents as shown in Table 2. The mutational landscape at diagnosis and relapse done via NGS was available in 104 patients (92%) and shown in Figure S1A,B.

Of 113 patients, 55 (48.7%) in our cohort achieved a CRc with CR in 25 patients (22.1%) and CRi + CRp in 30 patients (26.5%). The mOS for all patients was 7.0 months (SD ±0.7 months). The CRc rate based on the prior FLT3i was comparable: 53.9% CRc rate in patients who received midostaurin versus 41.2% in patients who received sorafenib (Figure S2). This was not statistically significant. There was no difference in mOS between prior midostaurin and sorafenib (7.8 months vs. 5 months $p = .2$). In a subset analysis of patients treated with 7+3 + midostaurin induction with or without consolidation (RATIFY regimen), gilteritinib resulted in a CRc rate of 58% and an mOS of 7.8 months. A trend toward a higher CRc rate was noted in patients treated with gilteritinib in combination regimens ($n = 26$) rather than as a single agent ($n = 30$; 64% vs. 43%, respectively, $p = .09$ using Chi-square test); however, no survival advantage for combination therapy was seen over single agent. Although mOS was not different in patients who underwent hematopoietic stem-cell transplant (HSCT) before initiation of gilteritinib therapy (7.4 months for transplant group vs. 7.1 months for none-transplant), patients who underwent HSCT after gilteritinib had a statistically significant improvement in mOS compared to patients who did not receive transplant; 12 months versus 5.2 months HR = 0.46 (95% CI 0. 2–0.6; Figure 1A).

Once post-gilteritinib HSCT data was censored, survival analysis was performed based on disease response. Patients who achieve CR

TABLE 1 Characteristics of the patients enrolled in the analysis

Patients' characteristics	All patients ($n = 113$)
Age-year	
Mean (SD)	58.3 (15.4)
Range	18–92
Female-no. (%)	65 (57.5%)
Race	
White no. (%)	66 (58.4%)
African American no. (%)	11 (9.7%)
Other no. (%)	36 (31.9%)
AML risk	
Low/Intermediate no. (%)	73 (64.6%)
High no. (%)	36 (31.9%)
FLT3 mutation subtype	
ITD no. (%)	95 (84.1%)
TKD no. (%)	5 (4.4%)
Mixed	9 (8%)
Prior FLT3i	
Midostaurin no. (%)	65 (57.5%)
Sorafenib no. (%)	34 (30%)
Other FLT3i no. (%)	14 (12.5%)
Stem cell transplant (SCT)	
Before gilteritinib no. (%)	49 (43.4%)
After gilteritinib no. (%)	24 (21.2%).
Response to frontline FLT3i	
Relapse no. (%)	45 (39.8%)
Refractory no. (%)	68 (60.2%)
Use of gilteritinib in the clinical trial	
On a trial no. (%)	53 (46.9%)
Commercial use no. (%)	60 (53.1%)
Additional treatment to gilteritinib	
Single agent no. (%)	71 (62.8%)
Combined with other agents no. (%)	42 (37.2%)

Note: AML risk was stratified by ELN risk stratification.
Abbreviations: AML, acute myeloid leukemia; ELN, European leukemia net; FLT3i, FLT3 inhibitor; ITD, Internal Tandem Duplication; TKD, Tyrosine Kinase Domaine mutation.

had the best overall survival compared to CRi + CRp and nonresponders (NR). After a median follow-up of 9 months, the mOS in the CR group was not reached compared to mOS of 7.4 months in CRi + CRh and 4.3 months in NR, this was statistically significant with a *p* value of .01 using log-rank test (the median follow-up for the whole cohort is 11 months). In the CR group, patients who achieved MRD-negative status by either MFC ($n = 11$) or by PCR ($n = 16$) had improved mOS compared with their respective MRD positive counterparts (Figure 1B). Patients with cMRD negative by both MFC and PCR ($n = 11$) had a 100% probability of survival. Dual modality MRD negativity was statistically significant in comparison to negative cMRD by only one method (MFC or PCR; $p = .0001$).

We evaluated the mutational status at diagnosis or relapse in its relation to the response and survival analysis. Overall survival was independent of ELN risk group with favorable/intermediate ELN versus poor risk (6.7 months vs. 4.3 months $p = .3$). Further analysis showed that the FLT3 mutation type (ITD vs. TKD) had no effect on gilteritinib response or overall survival (6.8 months vs. 7.1 months). The two most common co-mutations (*NPM1* and *DNMT3A*) did not affect response or survival in this analysis including a double positive mutation status. We noted the persistence of ASXL-1 ($N = 9$ at diagnosis and $N = 6$ at relapse), TP53 ($N = 3$ at diagnosis and $N = 2$ at relapse), and RUNX1 ($N = 15$ at diagnosis and $N = 12$ at relapse) mutations at diagnosis and relapse and these mutations did not affect mOS compared to wild type for each mutation (5.7 months vs. 7.1 months; Figure 1C). Interestingly,

TABLE 2 Types of combination therapies used with gilteritinib

Type of combination therapy	% of patients (*n*)	CRc rate in each group
In combination with high intensity chemotherapy (FLAG, CPX-351, CLIA, CLAG, MEC)	31% (13)	53.8% (7)
Hypomethlating agents (Decitabine or Azacitidine)	33% (14)	50% (7)
Single-agent Venetoclax or Venetoclax with HMA	31% (13)	76.9% (10)
In combination with IDH inhibitor	5% (2)	50% (1)

Abbreviations: CLAG, cladribine, cytarabine, and granulocyte colony-stimulating factor; CLIA, cladribine, idarubicin, and cytarabine; CRc, composite complete remission; FLAG: fludarabine, cytarabine, and granulocyte colony-stimulating factor; IDH, isocitrate dehydrogenase; MEC, mitoxantrone, etoposide, and cytarabine; HMA, hypomethylating agent.

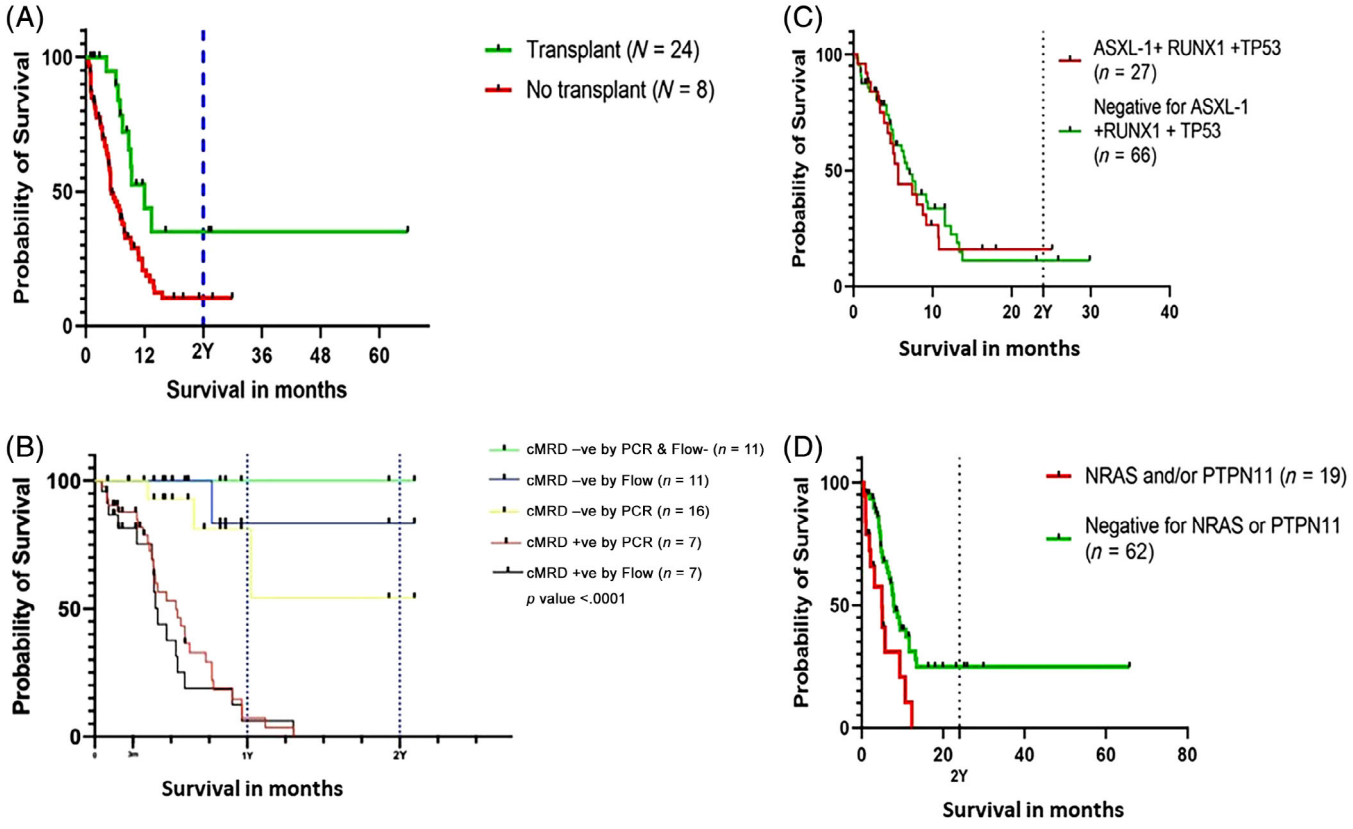

FIGURE 1 (A) Survival analysis via KM curves based on stem-cell transplant status. Survival is measured in months. (B) Survival analysis via KM curves based on clinical minimal residual disease (cMRD) testing. Flow refers to flow cytometry and PCR refers to FLT3 testing via polymerase chain reaction. (C) Survival analysis via KM curves based on any of three following mutations: ASXL, TP53, and RUNX1. (D) Survival analysis via KM curves based on mutations that activate MAPK kinase pathway (NRAS or PTPN11). KM, Kaplan–Meier; MAPK, mitogen-activated protein kinase [Color figure can be viewed at wileyonlinelibrary.com]

we also noted a new emergence of WT-1 mutation at relapse ($N = 11$); however, the emergence of this mutation did not affect response or overall survival. On the other hand, mutations that activate the MAPK kinase pathway and have been involved in gilteritinib resistance such as NRAS and PTPN11 were noted pre-gilteritinib therapy in ($N = 19$). The presence of these mutations had a nonsignificant inferior impact on CRc rate (59% vs. 37.5%) and mOS (4.9 months vs. 7.8 months; HR 2.4–95% CI 1. 1–5.4 -$p = .0057$; Figure 1D).

4 | DISCUSSION

This is the first and largest real-world study to confirm that gilteritinib retains its clinical activity in the setting of a prior FLT3i treatment. This multi-institutional analysis provides critical clinical information about the sequencing of different FLT3i outside of a clinical trial setting. In this data set, patients remained on gilteritinib for an average of 5.7 months and their chance of achieving CRc rate was 48.7% which is slightly lower than what is reported in ADMIRAL trial (54%), but this study provides a real-world experience with FLTi sequencing. Furthermore, an important clinical question that we addressed is CRc rate in patients with FLT3^{mut+} AML who relapse on 7+3 + midostaurin, with or without consolidation treatment. In this subgroup, gilteritinib produced a CRc rate of 58% and an mOS of 7.8 months. Overall, this is encouraging as our study exclusively included patients who relapsed or progressed on a prior FLT3i and drug resistance is always of a considerable fear for both the patients and physicians. Furthermore, multivariate analysis showed that FLT3 mutation type, ELN risk, and type of prior FLT3i used before did not affect the CRc rate and mOS. The patients who achieve CR had the best mOS out of CRc and most notably, cMRD negative by both PCR and flow cytometry had a 100% probability of survival with a median follow-up of 11 months. This is an interesting finding that requires validation in additional studies as the duration of gilteritinib therapy is not known and whether patients can eventually safely discontinue gilteritinib without undue risk of relapse is unclear. Typical of other studies in R/R AML, we also show that the use of HSCT is associated with prolonged mOS.

Our study is unique as it provides insights on the mutational landscape for these patients at diagnosis and relapse. Previous studies show that *NPM1* and *DNMT3A* mutations status affect prognosis in patients with FLT3^{mut+} AML. We show that *NPM1* and *DNMT3A* mutations status—while very prevalent in our patient population—did not affect gilteritinib response or mOS reflecting that relapsed or refractory AML has a poor prognosis regardless of these mutations. A trend toward worse outcomes was noted in ASXL1, TP53, and RUNX1 mutations, however, their prevalence was relatively low. Despite the emergence of WT-1 at relapse, this mutation at baseline had no effect on response or survival. We also interrogated various mutations that have been associated with gilteritinib resistance in other reports, such as mutations in the MAPK pathway. In this analysis, we confirm that NRAS and PTPN11 mutations—while seldom mutated at baseline—appear to be associated with worse survival compared to patients lacking these mutations. Thus, they may confer resistance to gilteritinib and thus alternative regimens for the treatment of patients and may warrant consideration of combination strategies or alternate regimens through clinical trials.

This retrospective analysis has some limitations. Most notably, the cMRD testing, which was defined clinically, was done at different institutions and not verified in a central lab. We acknowledge that it is not the standard sensitive MRD testing and the depth of MRD assessment is limited with sensitivities of these assays. However, these testing techniques have been ordered and interpreted by the treating physicians outside of the clinical trial setting, and incorporating them in our analysis did provide valuable clinical information. In addition, although our data included patients from 11 cancer centers, only five patients were African Americans which supports health and ethnic disparities that tertiary cancer centers face. This is a very important issue that needs to be addressed in future clinical trials.

In conclusion, this multicenter analysis is the first to show that gilteritinib remains a clinically active agent after treatment failure of prior FLT3i's, including in patients treated with the approved 7+3+ midostaurin regimen. We also confirm that mutations affecting the MAPK kinase pathway such as NRAS and PTPN11 appear to contribute to resistance to gilteritinib. Finally, factors associated with long-term survival to gilteritinib salvage include the use of subsequent transplant, FLT3 mutation clearance, and achievement of an MRD negative state by flow cytometry.

CONFLICT OF INTEREST

Zeidan: *Cardiff Oncology*: Consultancy, Honoraria, Other; *Trovagene*: Consultancy, Honoraria, Research Funding; *Pfizer*: Consultancy, Honoraria, Research Funding; *Otsuka*: Consultancy, Honoraria; *Abbvie*: Consultancy, Honoraria, Research Funding; *Boehringer-Ingelheim*: Consultancy, Honoraria, Research Funding; *Celgene/BMS*: Consultancy, Honoraria, Research Funding; *Jazz*: Consultancy, Honoraria; *Daiichi Sankyo*: Consultancy, Honoraria; *BeyondSpring*: Consultancy, Honoraria; *Seattle Genetics*: Consultancy, Honoraria; *Taiho*: Consultancy, Honoraria; *Cardinal Health*: Consultancy, Honoraria; *Acceleron*: Consultancy, Honoraria; *Astellas*: Consultancy, Honoraria; *Aprea*: Research Funding; *ADC Therapeutics*: Research Funding; *MedImmune/Astrazeneca*: Research Funding; *Takeda*: Consultancy, Honoraria, Research Funding; *Ionis*: Consultancy, Honoraria; *Epizyme*: Consultancy, Honoraria; *Astex*: Research Funding; *CCITLA*: Other; *Leukemia and Lymphoma Society*: Other; *Agios*: Consultancy, Honoraria; *Novartis*: Consultancy, Honoraria, Research Funding; *Incyte*: Consultancy, Honoraria, Research Funding. **Yilmaz**: *Pint Pharma*: Honoraria; *Pfizer*: Research Funding; *Daicho Sankyo*: Research Funding. **Foran**: *Agios*: Honoraria, Research Funding; *H3Biosciences*: Research Funding; *Xencor*: Research Funding; *Trillium*: Research Funding; *Takeda*: Research Funding; *Kura Oncology*: Research Funding; *Aptose*: Research Funding; *Aprea*: Research Funding; *Actinium*: Research Funding; *Boehringer Ingelheim*: Research Funding; *Abbvie*: Research Funding; *BMS*: Membership on an entity's Board of Directors or advisory committees; *Pfizer*: Membership on an entity's Board of Directors or advisory committees; *Servier*: Membership on an entity's Board of

Directors or advisory committees; *Novartis*: Membership on an entity's Board of Directors or advisory committees; *Revolution Medicine*: Consultancy. **Daver**: *Celgene*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Daiichi Sankyo*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Syndax*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Amgen*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *KITE*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Agios*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Bristol-Myers Squibb*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Pfizer*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Karyopharm*: Research Funding; *Servier*: Research Funding; *Genentech*: Research Funding; *AbbVie*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Astellas*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Novimmune*: Research Funding; *Gilead*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen*: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Trovagene*: Research Funding; *Fate Therapeutics*: Research Funding; *ImmunoGen*: Research Funding; *Novartis*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Jazz*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Trillium*: Consultancy, Membership on an entity's Board of Directors or advisory committees. **Perl**: *Novartis*: Honoraria, Other, Research Funding; *Agios*: Consultancy, Honoraria, Other; *Biomed Valley Discoveries*: Research Funding; *Jazz*: Honoraria, Other; *FORMA Therapeutics*: Consultancy, Honoraria, Other; *Syndax*: Consultancy, Honoraria; *Actinium Pharmaceuticals Inc*: Consultancy, Honoraria, Research Funding; *AbbVie Inc*: Consultancy, Honoraria, Other, Research Funding; *Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company*: Consultancy, Honoraria, Other; *Bayer HealthCare Pharmaceuticals*: Research Funding; *New Link Genetics*: Honoraria, Other; *Astellas*: Consultancy, Honoraria, Other: writing/editorial support, travel costs for meeting presentations related to study, Research Funding; *Daiichi Sankyo*: Consultancy, Honoraria, Other: Writing/editorial support, travel costs for meetings, Research Funding; *Leukemia & Lymphoma Society*, *Beat AML*: Consultancy; *Arog Pharmaceuticals Inc*: Other: uncompensated consulting, travel costs for meetings; *FUJIFILM Pharmaceuticals USA*, *Inc*: Research Funding; *Takeda*: Honoraria, Other: Travel costs for meeting. **Altman**: *Kartos*: Research Funding; *Celgene*: Research Funding; *Boehringer Ingelheim*: Research Funding; *ImmunoGen*: Research Funding; *Amgen*: Research Funding; *Aprea*: Research Funding; *Amphivena*: Research Funding; *Genentech*: Research Funding; *Novartis*: Consultancy; *Syros*: Consultancy; *Janssen*: Consultancy; *Immune Pharmaceuticals*: Consultancy; *ASH*: Consultancy; *Bristol-Myers Squibb*: Consultancy; *Glycomimetics*: Other: Data safety and monitoring committee; *Daiichi Sankyo*: Other: Advisory Board - no payment but was reimbursed for travel; *Kura Oncology*: Other: Scientific Advisory Board - no payment accepted, Research Funding; *BioSight*: Other: No payment but was reimbursed for travel, Research Funding; *AbbVie*: Other: advisory board, Research Funding; *Agios*: Other: advisory board, Research Funding; *Theradex*: Other: Advisory Board; *Astellas*: Other: Advisory Board, Speaker (no payment), Steering Committee (no payment), Research Funding; *PrIME Oncology*: Consultancy; *PeerView*: Consultancy; *Cancer Expert Now*: Consultancy; *France Foundation*: Consultancy; *Fujifilm*: Research Funding. **Off-label disclosure**: Some of the patients we are reporting on received gilteritinib in combination with other agents which is off-label use.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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