Real-World Brigatinib Dosing Patterns in Patients with Anaplastic Lymphoma Kinase Positive Non-Small Cell Lung Cancer in the United States

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DISCLOSURES

HML and YW are employees of Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, and may own stock. DRC has served as a consultant to AstraZeneca, Takeda, Arrys/Kyn, Genoptix, G1 Therapeutics (DSMB), Mersana Therapeutics, Roche/Genentech, Ignyta, Daichii Sankyo (ILD adjudication committee), Hansoh SRC, Bio-Thera DSMB, Lycera, Revolution Med, Orion, Clovis, Celgene, Novartis and has received research funding from ARIAD/Takeda. MG, CBM, WTH, and CCC are employees of IQVIA. IQVIA was paid by Takeda to conduct the current study.

STUDY SPONSORSHIP

Study was sponsored by Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Background

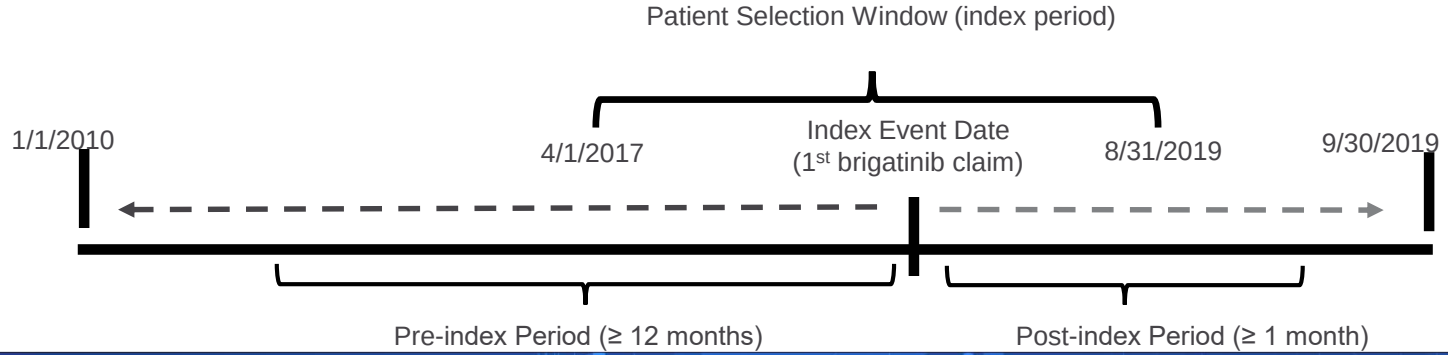
- Anaplastic lymphoma kinase (ALK) mutations occur in 3-5% of non-small cell lung cancer (NSCLC) cases[1]
- Brigatinib is a next-generation ALK inhibitor for treating ALK+ NSCLC
- Standard dosing of brigatinib is 90 mg once daily for 7 days then escalated to 180 mg on Day 8, as tolerated
- Among patients receiving this standard dose, 29% in the post-crizotinib ALTA trial and 38% in the tyrosine kinase inhibitor (TKI)-naïve ALTA-1L trial required a dose reduction.
  - Asymptomatic laboratory abnormalities including creatine phosphokinase, amylase or lipase elevations were common causes of dose reductions in these studies
- Outside of trial protocol mandated dosing, real-world dosing patterns of brigatinib have not been previously described

[1] Camidge DR, Kim HR, Ahn M, et al. (2020) Journal of Clinical Oncology. doi: 10.1200/JCO.20.00505

Study Design

- This retrospective cohort study utilized IQVIA's US-based Longitudinal Patient-Centric Pharmacy Claims Database (LRx), which includes prescription transaction data from pharmacies, payers, software providers and transactional clearinghouses
- All patients with a claim for brigatinib between 01-Apr-2017 and 31-Aug-2019 were identified for analysis. Patients were indexed to their first brigatinib claim
- Patients were ≥18 years of age on the index date, had at least 12 months of pre-index observation, and were continuously followed post-index until brigatinib discontinuation (≥ 90-day gap in brigatinib therapy or switch to another ALK TKI) or the end of follow-up (Figure 1)

Figure 1. Study schema



Methods

Average daily dose (ADD) and dose reduction

- ADD was calculated as the product of pill strength and quantity of pills dispensed divided by the days of supply
- Dose reduction was defined as ≥30 days of supply with ADD < 180 mg/day after reaching 180 mg/day, or < maximum (max) dose in patients who did not reach 180 mg/day.
- Time to dose reduction from 180 mg/day or max dose and probability of continued therapy at ≥180 mg/day or max dose were assessed via Kaplan-Meier analysis
- Reasons for dose modifications/non-escalation were not capturable

Methods

Adherence

- Medication possession ratio (MPR) was defined as the sum of the days' supply for all brigatinib claims while on treatment, divided by the treatment duration
  - Treatment duration was defined as the number of days between the start of brigatinib treatment to the earliest of: last day of supply, switch date, or end of follow-up.
- Adherence was defined as MPR ≥ 80%
- Dose compliance scores (DCS) were calculated as the sum of doses received from the first to the last prescription of brigatinib prior to discontinuation, divided by the perfect compliance dose (per label, i.e., 7 days at a dose of 90 mg/day followed by a maintenance dose of 180 mg/day for the duration of therapy)

Results

- A total of 240 patients were analyzed with 202 (84.2%) patients reaching a dose of ≥180 mg/day, of which 87.1% had received at least 1 ALK-TKI therapy prior to brigatinib initiation

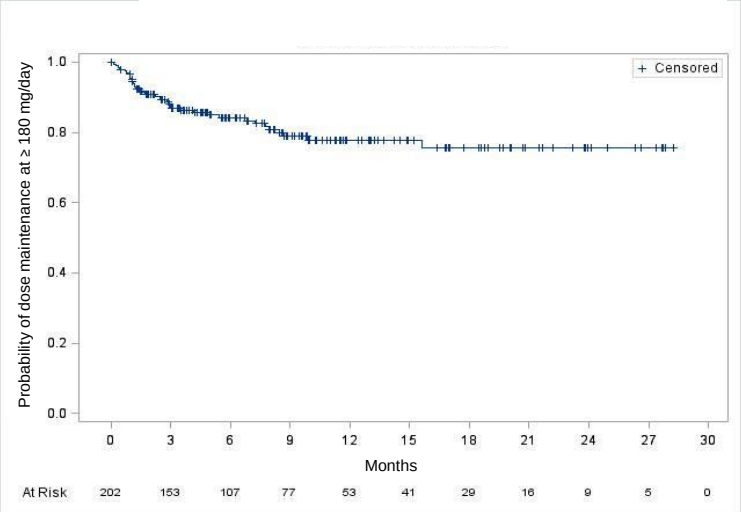
Table 1. Baseline characteristics of the sample

	All Brigatinib Patients N=240	Brigatinib patients who reach ADD ≥ 180 mg N=202	Brigatinib patients who never reach ADD ≥ 180 mg N=38	p-value[1]
Age, mean (SD)	57.9 (13.1)	65.6 (13.0)	64.9 (11.9)	0.0003
Female sex, n (%)	139 (57.9)	113 (55.9)	26 (68.4)	0.1528
Region, %				
Northeast	40 (16.7)	37 (18.3)	3 (7.9)	0.2676
Midwest	61 (25.4)	53 (26.2)	8 (21.1)	
South	54 (22.5)	46 (22.8)	8 (21.1)	
West	68 (28.3)	53 (26.2)	15 (39.5)	
Unknown	17 (7.1)	13 (6.4)	4 (10.5)	
Payer type, %				
Third Party	157 (65.4)	134 (66.3)	23 (60.5)	0.008
Medicaid	5 (2.1)	5 (2.5)	0 (0)	
Medicare Part D	76 (31.7)	63 (31.2)	13 (34.2)	
Cash	2 (0.8)	0 (0)	2 (5.3)	
Follow-up months, mean (SD)	10.7 (7.6)	11.0 (7.6)	9.2 (7.2)	0.1637

[1] p-value comparing brigatinib patients who did and did not reach a dose of 180 mg/day (n=202 vs. n=38)

Results (continued): patients who reached a dose of ≥ 180 mg/day

Figure 2. Time to brigatinib dose reduction in patients who reached a dose of ≥ 180 mg/day



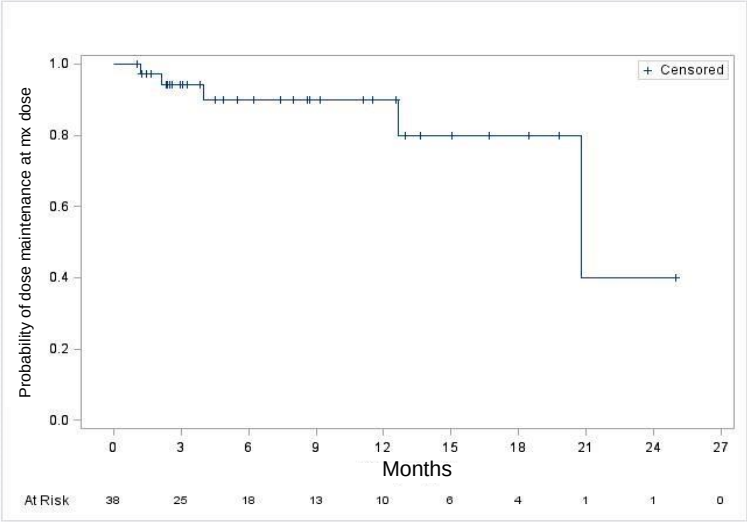
Time	N at Risk	Probability of Continued Therapy with Dose ≥ 180 mg/day
3 months	156	89.5%
6 months	104	86.0%
12 months	53	80.2%

Reduced Dose	N	%
<90 mg/day	6	18.8%
90 mg/day	7	21.9%
120 mg/day	14	43.8%
>120 mg/day	5	15.6%

- A total of 202 (84.2%) patients reached a dose of at least 180 mg/day, of which 87.1% were treated after 1+ prior lines.
- Of these 202 patients, 32 (15.8%) had a later dose reduction
- Of the patients with a dose reduction, the majority (59.4%) reduced to ≥ 120 mg/day

Results (continued): patients who did not reach a dose of ≥ 180 mg/day

Figure 3. Time to brigatinib dose reduction in patients who did not reach a dose of ≥ 180 mg/day



Time	N at Risk	Probability of Continued Therapy with Max Dose
3 months	25	94.1%
6 months	18	89.8%
12 months	10	89.8%

Reduced Dose	N	%
30 mg/day	1	20.0%
45 mg/day	1	20.0%
90 mg/day	2	40.0%
120 mg/day	1	20.0%

- In total, 38 (15.8%) patients did not reach 180 mg/day. Of these, 5 (13.2%) had a later dose reduction from their peak dose
- 50.0% of patients who did not reach 180 mg/day remained on a dose of 90 mg/day; while 21.1% reached a max dose of 159 mg/day. Among the patients with a dose reduction, the majority (60.0%) reduced to 90 or 120 mg/day

Results (continued): Brigatinib adherence and dose compliance

- Adherence and dose compliance were high overall and among patients who did and did not reach a dose of ≥ 180 mg/day

Table 2. Adherence and dose compliance

	All Brigatinib Patients N=240	Brigatinib patients who reach ADD ≥ 180 mg N=202	Brigatinib patients who never reach ADD ≥ 180 mg N=38
MPR (mean, SD)	1.0 (0.2)	1.0 (0.2)	1.0 (0.3)
% Adherent	93.3%	94.1%	89.5%
DCS (mean, SD)	1.0 (0.3)	1.0 (0.3)	0.7 (0.3)

ADD: average daily dose; mg: milligrams; MPR: medication possession ratio; SD: standard deviation; DCS: dose compliance score

Limitations and Conclusions

Limitations

- The LRx database does not include all specialty pharmacies that dispense brigatinib, potentially yielding a sample that is not necessarily representative of all brigatinib patients; Brigatinib dosing data may be limited by the fact that it was derived from days of supply, tablet strength, and quantity dispensed (vs. prescribing instructions). Reasons for dose modification/non-escalation were not capturable.

Conclusions

- Real-world data suggest that standard dose escalation (90 to 180 mg) occurs in most brigatinib patients (>84%)
- Dose reduction rates appear to be markedly lower in the real-world setting (15.8% for those reaching 180 mg) compared to those observed in clinical trials where specific dose reduction rules, including for asymptomatic lab changes, applied
- Brigatinib adherence and dose compliance were high
- Taken together, results from clinical trials and real-world evidence suggest brigatinib is efficacious, effective and well tolerated