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POSTER ABSTRACTS

902.HEALTH SERVICES AND QUALITY IMPROVEMENT - LYMPHOID MALIGNANCIES

Standard-of-Care Bortezomib Dosing in Multiple Myeloma: An International Survey of Physicians

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Background: Bortezomib (Velcade), a mainstay of treatment regimens for newly diagnosed multiple myeloma (MM), is often dosed twice-weekly in trials (i.e., Days 1, 4, 8, 11 in 21-day cycles). However, several analyses have shown that once-weekly bortezomib performs comparably and is associated with less peripheral neuropathy (Sidana PLoS One 2017, Mateos L&L 2020, Cook AJH 2021). Many centers thus use once-weekly bortezomib in MM induction regimens regardless of transplant eligibility, e.g. modified VRd or Dara-VRd in 28-day cycles with once-weekly subcutaneous (SC) bortezomib 1.3 mg/m ^{2} (McCaughan BJH 2022). Physician attitudes and perceptions regarding how bortezomib should be dosed, an important step toward establishing a global standard of care in MM, have not been investigated.

Methods: We conducted a global online survey of hematologists/oncologists who had treated ≥1 patient with MM in the past 12 months. The survey was distributed via social media platforms as well as targeted emails to MM physicians, IMWG members, and outreach through professional societies. The survey comprised 14 questions including usage of once- vs twice-weekly bortezomib, usage of SC vs IV bortezomib, attitudinal questions about potential benefits/disadvantages of each approach, and perceived barriers to using once-weekly bortezomib. Statistics were analyzed descriptively with Wilcoxon rank-sum and signed-rank tests.

Results: Of 317 webpage visits, 205 responses were recorded (65% completion rate).Most respondents were from US academic practices (25%, n=52), US community practices (22%, n=46), or Australian academic practices (6%, n=13); however, responses were recorded from 38 countries including 22 low- or middle-income countries (LMICs: 29% of responses, n=60).Over a third of respondents (37%, n=76) practiced in community settings, and most respondents (58%, n=119) reported >20 patients with MM under their personal care . 93 respondents (45%) had previously helped write institutional or societal guidelines, including 21 IMWG members.Respondents reported using once-weekly bortezomib most of the time (median 95% of patients, IQR 80%-100%) and almost always used SC bortezomib (IQR 100%-100%).There were no significant differences in bortezomib frequency or route based on academic vs community practice, experience with MM, US vs non-US, or LMIC vs non-LMIC.

Large majorities of respondents (Table 1) felt that once-weekly bortezomib is preferred by patients (94%), associated with comparable durations of response (79%), and associated with less peripheral neuropathy (89%). Conversely, 61% of respondents felt that twice-weekly bortezomib in superior in newly diagnosed MM with acute cast nephropathy.Physician estimates of the incidence of any-grade peripheral neuropathy were significantly lower with once-weekly bortezomib (median 30%, IQR 20-43%) vs twice-weekly bortezomib (median 50%, IQR 40-73%). Similarly, Grade 3+ neuropathy estimates were significantly lower with once-weekly (median 10%, IQR 5-17%) vs twice-weekly bortezomib (median 25%, IQR 15-38%), with $p<0.001$ in all cases . The most common cited barriers to ordering once-weekly bortezomib (Table 2) were perceived lack of prospective data (31%), difficulty modifying treatment orders (24%), and resistance from pharmacist colleagues who prefer adhering to trial-studied regimens (13%).

Discussion: In our survey of over 200 MM-treating physicians from 38 countries (including 22 LMICs), once-weekly subcutaneous bortezomib was overwhelmingly preferred regardless of practice setting or country. The only exception was acute

cast nephropathy, where twice-weekly bortezomib may expedite renal recovery and is reasonable to use initially. Neuropathy estimates were similar to published incidences (32% with once-weekly bortezomib vs 47% with twice-weekly bortezomib) from prospective data collected from the ALCYONE, GIMEMA-QW, and VISTA randomized trials (Mateos L&L 2020). Our findings highlight the widening mismatch between what physicians routinely prescribe to patients versus what registrational trials typically require. Given that >90% of physicians personally prefer once-weekly bortezomib and that >90% report that their patients feel similarly, once-weekly bortezomib appears to have become the global standard of care. This consensus should be taken into consideration for clinical trial design in the future.

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Table 1: Physician attitudes regarding once-weekly bortezomib

Compared to twice-weekly bortezomib, once-weekly bortezomib….	**Agree** % (n)	**Disagree** % (n)	**Unsure** % (n)
Has comparable durations of responses.	79% (160)	5% (11)	16% (32)
Has lower rates of peripheral neuropathy.	89% (182)	4% (8)	7% (14)
Is generally preferred by patients.	94% (191)	2% (5)	4% (8)
Has inferior pharmacokinetics.	19% (38)	45% (92)	37% (75)
Is harder to get insurance/regulatory approval for.	7% (15)	54% (110)	39% (79)
Is inferior for patients with acute cast nephropathy.	61% (125)	16% (32)	23% (47)

Table 2: Stated barriers to once-weekly or subcutaneous bortezomib

Do these factors pose barriers to ordering once-weekly or subcutaneous bortezomib?	**Not a barrier** % (n)	**Barrier** % (n)	**Unsure** % (n)
(Once-weekly) Lack of prospective data	66% (134)	31% (63)	3% (7)
(Once-weekly) Difficulty modifying orders	77% (155)	24% (47)	0% (0)
(Once-weekly) Pharmacists prefer trial's regimen	86% (177)	13% (27)	0% (1)
(Once-weekly) Lost clinic revenue	93% (190)	4% (9)	2% (5)
(Subcutaneous) Lack of prospective data	86% (176)	11% (23)	3% (6)
(Subcutaneous) Difficulty modifying orders	91% (186)	7% (14)	2% (4)
(Subcutaneous) Too expensive	94% (189)	5% (10)	1% (3)
(Subcutaneous) Not available in country	95% (194)	3% (7)	2% (4)

Figure 1

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