Abstract: P917

Title: LISAFTOCLAX (APG-2575) COMBINED WITH NOVEL THERAPEUTIC REGIMENS IN PATIENTS (PTS) WITH RELAPSED OR REFRACTORY (R/R) MULTIPLE MYELOMA (MM) OR IMMUNOGLOBULIN LIGHT-CHAIN (AL) AMYLOIDOSIS

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

R/R MM is incurable, with virtually inevitable relapse without appropriate therapeutic interference. AL amyloidosis is a rare disease that may cause serious illness or death. Lisaftoclax is a novel, investigational, potent, selective BCL-2 inhibitor with clinical benefits in hematologic malignancies and solid tumors with a low reported incidence of adverse events (AEs) (Ailawadhi et al. *Clin Cancer Res.* 2023;29:2385-93).

Aims:

The aim of this multicenter study was to evaluate the safety and efficacy of lisaftoclax combined with pomalidomide and dexamethasone (Arms A and C) or daratumumab, lenalidomide, and dexamethasone (Arm B) in pts with R/R MM (Arm A and B) or R/R AL amyloidosis (Arm C).

Methods:

Eligible pts provided informed consent and had an ECOG performance status ≤ 2, ≥ 1 prior line of therapy, and adequate organ function. Pts with R/R AL amyloidosis had confirmed symptomatic organ involvement, purpura, and/or carpal tunnel syndrome. Lisaftoclax was administered orally daily at various doses in repeated 28-day cycles. Pomalidomide, daratumumab, and lenalidomide were administered per label use. Dexamethasone 40 mg (20 mg, pts aged > 75 years) was administered on Days 1, 8, 15, and 22 of 28-day cycles.

Results:

As of January 25, 2024, 44 pts were enrolled including 36 R/R MM and 8 R/R AL amyloidosis: 30 in Arm A at dose levels of 400 (n = 3), 600 (n = 4), 800 (n = 11), 1,000 (n = 6), and 1,200 mg (n = 6); 6 in Arm B at 600 mg; and 8 in Arm C at 400 (n = 1), 600 (n = 4), and 800 mg (n = 3). The median (range) age of pts was 70.5 (24-88) years, 68.2% were male, and 65.9% older than 65. The median (range) number of prior therapy lines was 3 (1-19), median (range) time from diagnosis to first dose of study drug was 5.5 (129) years, and median (range) number of treatment cycles, 4 (1-26). A total of 29 pts were triple-class-exposed, 11 had received pomalidomide, and 4 harbored t(11;14) at baseline. Of 42 pts in the safety analysis population, 30 reported any-grade lisaftoclax treatment-related AEs (TRAEs; ≥ 5% incidence), including neutropenia (23.8%), nausea (19.0%), leukopenia (9.5%), abdominal distension (9.5%), diarrhea (9.5%), and constipation (7.1%). Ten pts experienced grade ≥ 3 TRAEs, including neutropenia (14.3%) and febrile neutropenia (2.4%), and 3 experienced lisaftoclax-related serious AEs: febrile neutropenia, acute kidney injury, and diarrhea and electrolyte imbalance (1 each). In Arm B, 1 pt experienced a dose-limiting toxicity (prolonged QT interval). A total of 24 pts discontinued treatment because of disease progression (n = 15), TEAE (n = 3), nonadherence (n = 1), or investigator/pt decision (n = 5). In Arm A, 27 pts with R/R MM were efficacy evaluable, of whom 10 had partial response (PR), 7 very good PR (VGPR), and 2 complete response (CR). The overall response rate (ORR [PR or better]) was 70.4%, with a median (range) time to response of 1.0 (1-3) months. Two pts with R/R MM in Arm B achieved a CR, and the median (range) time to response was 1.4 (1-2) months. In Arm C, 7 pts with R/R AL amyloidosis were efficacy evaluable, and the hematologic ORR (VGPR or better) was 85.7% (3 VGPR; 1 each of unconfirmed VGPR, CR, and stringent CR). The median (range) time to response was 0.9 (1-4) month, and 2 pts experienced organ function improvement.

Conclusion:

Lisaftoclax plus novel therapeutic regimens was well tolerated and demonstrated preliminary antitumor activity in both pts with R/R MM or AL amyloidosis. ClinicalTrials.gov registration/internal study ID: NCT04942067/APG2575MU101.

Keywords: Multiple myeloma, AL amyloidosis, BCL2, Safety