Supplemental Material

Eligibility Criteria

Key Inclusion Criteria

- Males and females ≥18 years of age
- Tumor type
    - Relapsed/refractory non-Hodgkin lymphoma (NHL) that met one of the following criteria:
        - Diffuse large B-cell lymphoma (DLBCL) or transformed follicular lymphoma (FL) relapsed after, or refractory to at least one prior chemotherapy regimen (eg, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone [R-CHOP]) AND not a candidate for standard salvage regimens or autologous stem cell transplant (eg, due to age, comorbid conditions, or failure to respond to salvage chemotherapy). Local confirmation of lymphoma subtype (eg, germinal center B-cell [GCB]-DLBCL) was allowed for enrollment but must have been confirmed through central laboratory testing
        - DLBCL or transformed FL relapsed after or refractory to at least two prior chemotherapy regimens
        - Other NHLs that had failed at least one prior line of therapy and for which there was no standard salvage regimen
    - Patients with relapsed and/or refractory multiple myeloma who have failed prior standard therapy and for which there is no standard salvage regimen

    - Solid tumors (evaluable by Response Evaluation Criteria in Solid Tumors [RECIST] criteria), with the exception of castrate-resistant prostate cancer (CRPC), at least one and not more than three standard-of-care chemotherapeutic regimens, or tumor for which there is no approved therapy, or for which standard therapy is refused
- DLBCL and transformed FL: Availability of archival tissue, or willingness to undergo fresh biopsy for: confirmation of GCB-DLBCL status (DLBCL patients); retrospective central testing of enhancer of zeste homolog 2 (EZH2) mutation status (DLBCL and transformed FL patients). For all other tumor types: availability of either archival tissue or fresh biopsies
- Must have a pre-existing central venous access such as a port, Hickmann catheter, or a peripherally inserted central catheter (PICC line) or be willing and able to have one inserted
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Patients with child-bearing potential must agree to use one of the contraceptive methods
- Normal hematologic, hepatic, renal, reproductive, endocrine, and heart function

<u>Key Exclusion Criteria</u>

- Patients currently receiving cancer therapy (chemotherapy, radiation therapy, immunotherapy, or biologic therapy)
- Patients who received an investigational anti-cancer drug within 4 weeks, or within 5 half-lives (whichever is shorter) of the first dose of study drug. Any major surgery, radiotherapy, or immunotherapy within the 4 weeks prior to first dose of

study drug or palliative radiotherapy to a single symptomatic lesion within the 2 weeks prior to first dose of study drugs

- Patients who previously received an autologous stem cell transplant were allowed if a minimum of 100 days had elapsed from the time of transplant and the patient had recovered from transplant-associated toxicities prior to the first dose of GSK2816126
- Chemotherapy regimens with delayed toxicity within the 3 weeks prior to first dose of study drug. Chemotherapy regimens given continuously or on a weekly basis with limited potential for delayed toxicity within 2 weeks prior to first dose of study drugs
- Unresolved toxicity greater than grade 1 (National Cancer Institute – Common Terminology Criteria for Adverse Events [NCI-CTCAE] version 4) from previous anti-cancer therapy, with the exception of alopecia and peripheral neuropathy
- Cardiac exclusion criteria included history of acute coronary syndromes (including myocardial infarction and unstable angina), coronary angioplasty, or stenting within the past 6 months prior to first dose of study drug, QTc interval >450 msec, uncontrolled arrhythmias or class II, III, or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system
- Current use of a prohibited medication or an expectation to require any of those medications during treatment with study drugs
- Uncontrolled diabetes or other medical condition that may have interfered with assessment of toxicity

- Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to the study drug or their excipients
- Psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol

Withdrawal Criteria

Patients received study treatment until disease progression, death, or unacceptable toxicity, including meeting stopping criteria for liver chemistry, was reached. In addition, study treatment was permanently discontinued for any of the following reasons:

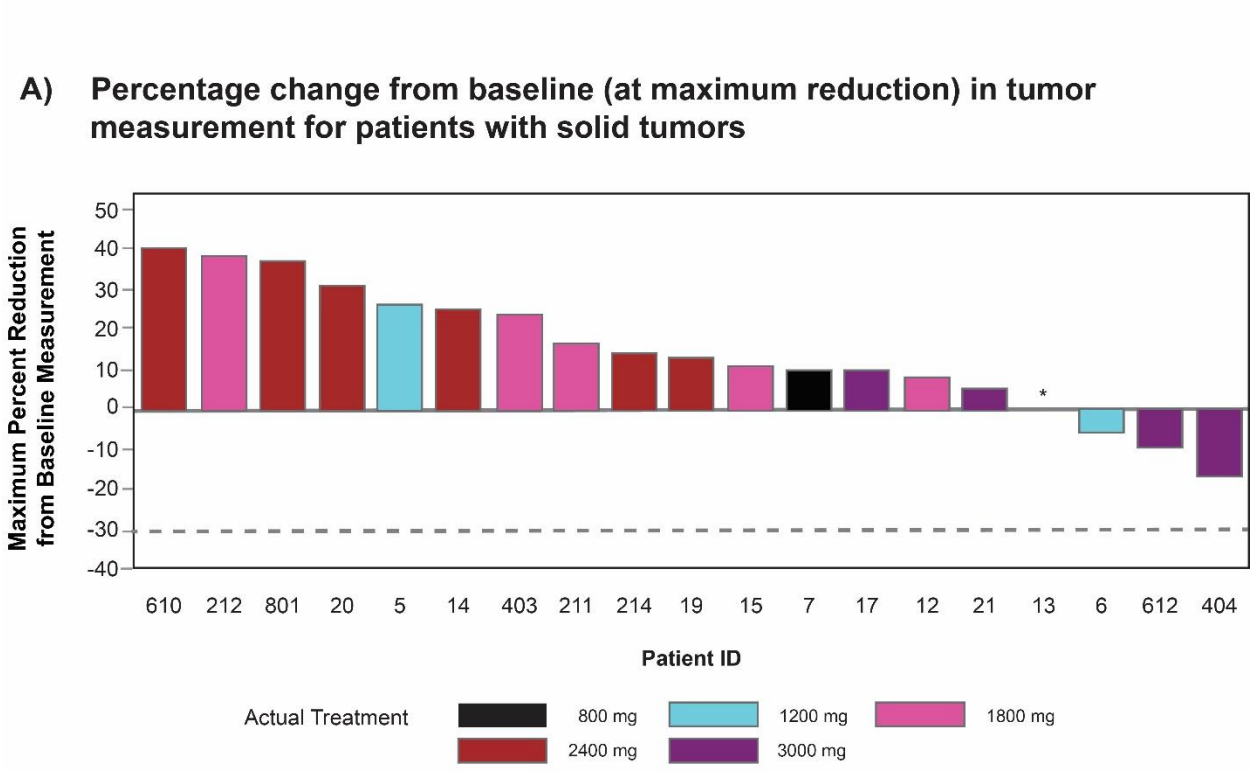
- Substantial deviation(s) from the protocol
- Request of the patient or proxy. If the patient voluntarily discontinued from treatment due to toxicity, “adverse event” was to be recorded as the primary reason for permanent discontinuation on the electronic case report form
- Investigator’s discretion
- A dose delay of >21 days unless the Investigator and GlaxoSmithKline Medical Monitor agreed that further treatment may benefit the patient
- Intercurrent illness that prevented further administration of study treatment(s)
- Patient was lost to follow-up or study was closed or terminated
- Female patient who became pregnant while on study treatment
- During the follow-up phase, patients were followed for 30 days following the last dose of study drug

Supplemental Table 1. Summary of adverse events

	50 mg (N = 2)	100 mg (N = 1)	200 mg (N = 1)	400 mg (N = 1)	800 mg (N = 3)	1200 mg (N = 4)	1800 mg (N = 10)	2400 mg (N = 12)	3000 mg (N = 7)	Total (N = 41)
Any event (all patients)	2 (100)	1 (100)	1 (100)	1 (100)	3 (100)	4 (100)	10 (100)	12 (100)	7 (100)	41 (100)
AEs in ≥3 patients										
Fatigue	0	1 (100)	1 (100)	1 (100)	2 (67)	2 (50)	6 (60)	7 (58)	2 (29)	22 (54)
Nausea	1 (50)	0	0	0	2 (67)	2 (50)	3 (30)	9 (75)	3 (43)	20 (49)
Alanine aminotransferase increased	0	0	0	0	0	0	3 (30)	6 (50)	5 (71)	14 (34)
Anemia	0	0	0	1 (100)	2 (67)	0	3 (30)	6 (50)	1 (14)	13 (32)
Vomiting	0	0	0	0	2 (67)	2 (50)	2 (20)	2 (17)	3 (43)	11 (27)
Cough	1 (50)	0	0	0	0	0	6 (60)	1 (8)	0	8 (20)
Aspartate aminotransferase increased	0	0	0	0	0	0	1 (10)	3 (25)	3 (43)	7 (17)
Constipation	1 (50)	0	0	0	1 (33)	1 (25)	2 (20)	1 (8)	1 (14)	7 (17)
Infusion-related reaction	0	0	0	0	1 (33)	1 (25)	0	2 (17)	3 (43)	7 (17)
Pyrexia	0	0	1 (100)	0	0	2 (50)	0	2 (17)	2 (29)	7 (17)
Decreased appetite	1 (50)	0	1 (100)	0	1 (33)	0	1 (10)	1 (8)	1 (14)	6 (15)
Diarrhea	0	0	0	0	1 (33)	1 (25)	1 (10)	2 (17)	1 (14)	6 (15)
Hyperglycemia	1 (50)	0	0	0	0	1 (25)	1 (10)	2 (17)	1 (14)	6 (15)
Abdominal pain	0	0	0	0	1 (33)	2 (50)	0	0	2 (29)	5 (12)
Oral paresthesia	0	0	0	0	1 (33)	0	1 (10)	2 (17)	1 (14)	5 (12)
Tumor pain	0	0	0	0	2 (67)	1	0	2 (17)	0	5 (12)
Back pain	0	0	0	0	0	0	0	3 (25)	1 (14)	4 (10)
Blood alkaline phosphatase increased	0	0	0	0	1 (33)	0	1 (10)	1 (8)	1 (14)	4 (10)
Dyspnea	1 (50)	0	0	0	1 (33)	0	1 (10)	0	1 (14)	4 (10)
Hypokalemia	0	0	0	0	0	0	0	3 (25)	1 (14)	4 (10)
Hypomagnesemia	0	0	0	0	0	0	1 (10)	1 (8)	2 (29)	4 (10)
Peripheral edema	0	0	0	0	1 (33)	0	0	2 (17)	1 (14)	4 (10)
Pruritus	0	1 (100)	0	0	1 (33)	0	0	1 (8)	1 (14)	4 (10)
Thrombocytopenia	0	0	0	0	1 (33)	0	0	2 (17)	1 (14)	4 (10)

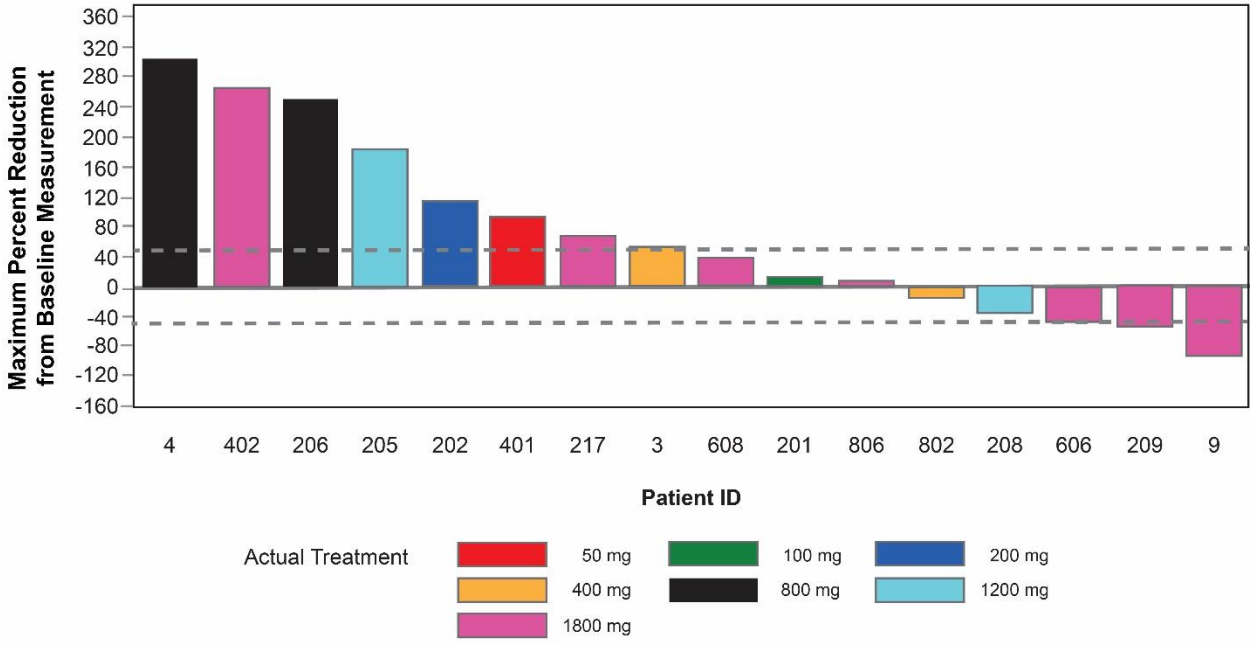
AE, adverse event.

Supplemental Figure 1 (A and B):



Note: An asterisk indicates the maximum reduction from baseline is 0%.
Note: Patients are not included in the figure if the target lesions are not assessed post-baseline.
Note: Percentage changes are based on target lesion.
Note: Patients 216 and 613 are not presented due to missing post-baseline lesion measurement.

B) Percentage change from baseline (at maximum reduction) in tumor measurement for patients with lymphomas



Note: Patients are not included in the figure if the target lymph node lesions are not assessed post-baseline.
Note: Percentage changes are based on target lesion.
Note: Patients 2, 22, 405, and 808 are not presented due to missing post-baseline lesion measurement.