*SUPPLEMENTAL INFORMATION FOR:*

**A phase 1b/2 study of the BRAF inhibitor encorafenib plus the MEK inhibitor binimetinib in patients with *BRAFV600E/K*-mutant solid tumors**

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Supplementary Table S1 Baseline patient and disease characteristics for phase 2 portion of study.

|  | BRAF V600 mutant mCRC N=11 | BRAF mutant melanoma progressed post BRAF inhibitor N=26 | BRAF mutant melanoma no prior BRAF inhibitor N=42 | All Patients N=79 |
| --- | --- | --- | --- | --- |
| **Age (Years)** |  |  |  |  |
| Median | 55.0 | 53.5 | 55.5 | 55.0 |
| Minimum | 43 | 25 | 23 | 23 |
| Maximum | 75 | 81 | 86 | 86 |
| **Sex, n (%)** |  |  |  |  |
| Female | 3 (27) | 11 (42) | 12 (29) | 26 (33) |
| Male | 8 (73) | 15 (58) | 30 (71) | 53 (67) |
| **Predominant Race, n (%)** |  |  |  |  |
| Caucasian | 11 (100) | 24 (92) | 37 (88) | 72 (91) |
| Black | 0 | 0 | 0 | 0 |
| Asian | 0 | 1 (4) | 0 | 1 (1) |
| Other | 0 | 1 (4) | 5 (12) | 6 (8) |
| **Ethnicity, n (%)** |  |  |  |  |
| Hispanic/Latino | 0 | 2 (8) | 1 (2) | 3 (4) |
| Not Hispanic or Latino | 11 (100) | 24 (92) | 41 (98) | 76 (96) |
| **ECOG performance status, n(%)** |  |  |  |  |
| 0 | 6 (55) | 13 (50) | 31 (74) | 50 (63) |
| 1 | 5 (45) | 12 (46) | 11 (26) | 28 (35) |
| 2 | 0 | 1 (4) | 0 | 1 (1) |

Supplementary Table S2: Baseline characteristics of patients with BRAF inhibitor–naive, *BRAF*-mutant melanoma

|  |  |
| --- | --- |
| **Baseline characteristic** | **N=55** |
| **Age, years at screening**  Median  Range | 54.0  23.0–86.0 |
| **Sex, n (%)**  Male  Female | 36 (66)  19 (35) |
| **Geographic region, n (%)**  North America  Asia-Pacific  Western Europe | 31 (56)  3 (6)  21 (38) |
| **Baseline LDH, n (%)**  ≤ULN  >ULN  Missing | 32 (58)  21 (38)  2 (4) |
| **ECOG PS, n (%)**  0  1 | 41 (74)  14 (26) |
| **BRAF subtype, n (%)**  V600E  V600K  Other | 49 (89)  5 (9)  1 (2) |
| **Tumour stage\*, n (%)**  IIIc  IVa  IVb  IVc | 2 (4)  8 (15)  10 (18)  35 (64) |
| **Initial encorafenib dose, n (%)**  50 mg QD  100 mg QD  200 mg QD  400 mg QD  450 mg QD  600 mg QD  800 mg QD | 3 (6)  1 (2)  1 (2)  2 (4)  7 (13)  39 (71)  2 (4) |

ECOG PS=Eastern Cooperative Oncology Group performance status. LDH=lactate dehydrogenase. QD=once daily. ULN=upper limit of normal.  
\*Based on sponsor assessments.

**Supplementary Table S3:** Efficacy as defined by Response Evaluation Criteria In Solid Tumors version 1.1

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Phase 2 Cohorts** | | |  | **All BRAFi-Naïve Melanoma Patients (Phase 1b/2)** | | |
|  | **BRAF V600 mutant mCRC  (n=11)** | **BRAF mutant melanoma progressed post BRAF inhibitor  (n=26)** | **BRAF mutant melanoma no prior BRAF inhibitor  (n=42)** |  | **Encorafenib 400/450 mg QD plus binimetinib 45 mg BID**  **(n=9)** | **Encorafenib 600 mg QD plus binimetinib 45 mg BID  (n=39)** | **All BRAFi-Naïve Melanoma Patients\*  (n=55)** |
| **CR‡, n (%)** | 0 | 1 (4) | 2 (5) |  | 1 (11) | 2 (5) | 6 (11) |
| **PR‡, n (%)** | 2 (18) | 10 (39) | 26 (62) |  | 6 (67) | 25 (64) | 34 (62) |
| **SD, n (%)** | 5 (46) | 8 (31) | 12 (29) |  | 2 (22) | 10 (26) | 13 (24) |
| **PD, n (%)** | 3 (27) | 4 (15) | 2 (5) |  | 0 | 2 (5) | 2 (4) |
| **Unknown** | 1 (9) | 3 (12) | 0 |  | 0 | 0 |  |
| **ORR, n (%) [95% CI]§** | 2 (18)  (2 - 52) | 11 (42)  (23 - 63) | 28 (67)  (51 - 80) |  | 7 (78) [40–97] | 27 (69) [52–83] | 40 (73) [59–84] |
| **DCR, n (%) [95% CI]§** | 7 (64)  (31 - 89) | 19 (73)  (52 - 88) | 40 (95)  (84 - 99) |  | 9 (100)  [66–100] | 37 (95) [83–99] | 53 (96) [88; 100] |

BID=twice daily. CR=complete response. DCR=disease control rate. ORR=overall response rate. PD=progressive disease. PR=partial response. QD=once daily. SD=stable disease.

\*Seven patients received a dose other than encorafenib 400/450 mg QD plus binimetinib 45 mg BID or encorafenib 600 mg QD plus binimetinib 45 mg BID.

‡Response confirmation is required.  
§Estimate (95% CI) for ORR and DCR were obtained using exact binomial confidence intervals.