*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 mCRCN=11 | BRAF mutant melanomaprogressed postBRAF inhibitorN=26 | BRAF mutant melanomano prior BRAFinhibitorN=42 | All PatientsN=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**MedianRange | 54.023.0–86.0 |
| **Sex, n (%)**MaleFemale | 36 (66)19 (35) |
| **Geographic region, n (%)**North AmericaAsia-PacificWestern Europe | 31 (56)3 (6)21 (38) |
| **Baseline LDH, n (%)**≤ULN>ULNMissing | 32 (58)21 (38)2 (4) |
| **ECOG PS, n (%)**01 | 41 (74)14 (26) |
| **BRAF subtype, n (%)**V600EV600KOther | 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 QD100 mg QD200 mg QD400 mg QD450 mg QD600 mg QD800 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 melanomaprogressed postBRAF inhibitor (n=26)**  | **BRAF mutant melanomano prior BRAFinhibitor (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.