**SUPPLEMENTARY MATERIAL**

**Supplementary Tables**

Supplementary Table 1. Number of treatment cycles administered by platinum therapy.

|  |  |  |
| --- | --- | --- |
| **Cycles administered** | **Cisplatin (N = 16)** | **Carboplatin (N = 11)** |
| **1** | 1 | 2 |
| **2** | - | 3 |
| **3** | 2 | 2 |
| **4** | 6 | 2 |
| **5** | - | 2 |
| **6** | 7 | - |

Supplementary Table 2. Treatment discontinuation/withdrawal reasons by platinum therapy.

|  |  |  |  |
| --- | --- | --- | --- |
| **Reason** | **Cisplatin (N = 16)** | **Carboplatin (N = 11)** | **Total (N = 27)** |
| Disease progression | 9 | 2 | 11 |
| Clinical decision | 1 |  | 1 |
| Patient choice |  | 5 | 5 |
| Unacceptable/Serious Adverse Event | 2\* | 3\*\* | 5 |
| Treatment Delay > 28 days | 3 | 1 | 4 |
| End of study – no further drug available | 1 |  | 1 |

*\*Grade 2 vomiting and Grade 3 dyspnoea (1 patient); Grade 2 diarrhea (1 patient)*

*\*\*Grade 2 infusion-related reactions (2 patients); Grade 3 infection (1 patient)*

Supplementary Table 3. Dose-limiting toxicities observed in the dose-escalation cohorts.

|  |  |  |  |
| --- | --- | --- | --- |
| **Platinum therapy and ganetespib dose (mg/m2)** | **Number of patients** | **Number of DLTs\*** | **DLT event (Cycle number)** |
| **Cisplatin** |  |  |  |
| 100 | 4 | 0 |  |
| 150 | 3 | 0 |  |
| 200 | 9 | 1 | G3 Nausea (Cycle 1) |
| **Carboplatin** |  |  |  |
| 100 | 1 | 0 |  |
| 150 | 1 | 0 |  |
| 200 | 9 | 2 | G2 Infusion-related reaction (Cycle 1)  G3 Nausea (Cycle 1) |

*Abbreviations: DLT, Dose-Limiting Toxicity.*

*\*Cycles 1 and 2 for the cisplatin cohort; and cycle 1 for the carboplatin cohort.*

Supplementary Table 4: Mean (SD) of genomic variables across baseline characteristics (n = 11).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** |  | **Total SCNA** | **Total LOH** | **Total Homozygous Deletions** |
| Sex |  |  |  |  |
|  | Female (n = 1) | 168 (-) | 38 (-) | 2 (-) |
|  | Male (n = 10) | 85.3 (63.9) | 20.9 (13.1) | 3.1 (3.1) |
| Histology |  |  |  |  |
|  | Epithelioid (n = 10) | 97.9 (66.7) | 19.4 (9.3) | 3.3 (3.0) |
|  | Non-epithelioid (n = 1) | 42 (-) | 53 (-) | 0 (-) |
| ECOG Performance Status | |  |  |  |
|  | 0 (n = 4) | 84.8 (71.9) | 30.3 (20.0) | 3.3 (4.6) |
|  | 1 (n = 7) | 97.4 (67.1) | 18 (6.0) | 2.9 (2.1) |
| EORTC Prognostic Score | |  |  |  |
|  | Good (n = 2) | 89 (111.7) | 22 (22.6) | 1.5 (0.7) |
|  | Poor (n = 9) | 93.7 (61.6) | 22.6 (12.7) | 3.3 (3.2) |
| Platinum Treatment | |  |  |  |
|  | Cisplatin (n = 5) | 85.8 (83.7) | 23.4 (17.7) | 2.4 (2.8) |
|  | Carboplatin (n = 6) | 98.7 (53.7) | 21.7 (10.4) | 3.5 (3.3) |
| Ganetespib dose (mg/m2) | |  |  |  |
|  | 100 (n = 3) | 72 (34.0) | 31.3 (18.8) | 3.7 (3.5) |
|  | 200 (n = 8) | 100.6 (74.5) | 19.1 (10.5) | 2.8 (3.0) |

*Abbreviations: SD, Standard Deviation; ECOG, Eastern Cooperative Oncology Group; EORTC, European Organisation for Research and Treatment of Cancer; SCNA, Somatic Copy Number Alterations; LOH, Loss of Heterozygosity.*

Supplementary Table 5: Mean (SE) of genomic variables per best response category.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Partial Response (N = 6)** | **Stable Disease (N = 1)** | **Not Evaluable (N = 4)** |
| Total SCNA | 105.5 (28.9) | 42 (-) | 86.5 (34.4) |
| Total LOH | 18.5 (2.8) | 53 | 20.8 (6.6) |
| Total Homozygous Deletions | 3.5 (1.4) | 0 | 3 (1.4) |

*Abbreviations: SE, Standard Error; SCNA, Somatic Copy Number Alterations; LOH, Loss of Heterozygosity.*

**Supplementary Figures**

Supplementary Figure 1. Progression-free survival in all patients.



Supplementary Figure 2. Progression-free survival by platinum treatment cohort.



Supplementary Figure 3. Progression-free survival by ganetespib dose.



Supplementary Figure 4. Overall survival in all patients.



Supplementary Figure 5. Overall survival by platinum treatment cohort.



Supplementary Figure 6. Overall survival by ganetespib dose.



Supplementary Figure 7. Best reduction in total tumour burden from baseline (%) by baseline genomic measurements and ganetespib dose.



*Abbreviations: SCNA, Somatic Copy Number Alterations; LOH, Loss of Heterozygosity.*