**Supplementary tables- Guichard *et al.***

**Supplementary table 1: Biochemical and cellular activity of AZD2014**.

AZD2014 was tested against isolated enzymes in biochemical assays or in MDAMB468 cells, using an Acumen laser scanning cytometer (TTP Labtech, UK) to analyse the levels of phosphorylation of S6 (Ser235/236) and AKT (Ser473).

|  |  |
| --- | --- |
| **Isolated enzyme** | **IC50 (nM)** |
| **mTOR** | **2.81** |
| **PI3K** | **3766** |
| **PI3K** | **>30000** |
| **PI3K** | **>29000** |
| **PI3K** | **>30000** |
|  | |
| **MDAMB468 cells** | **IC50 (nM)** |
| **pAKT (Ser473)** | **78** |
| **pS6 (Ser235/6)** | **210** |

**Supplementary table 2: Biochemical activity of AZD2014**.

AZD2014 (1 µM) was tested against 393 isolated kinases or catalytic domains in competition binding assays (Ambit). The % inhibition values are shown when >0%.

|  |  |
| --- | --- |
| **Kinase** | **% inhibition at 1M** |
| Dyrk2 | 47 |
| IKK | 34 |
| PIK3CA | 24 |
| PIK3CA (E545A) | 19 |
| PIK3CA (E545K) | 36 |
| PIK3CA (Q546K) | 21 |
| PIK3CA (E542K) | 21 |

**Supplementary table 3: Anti proliferative activity of AZD2014 in a panel of ER+, endocrine resistant and LTED cell lines.** GI50 (the concentration decreasing cell number by 50% compared to untreated cells) and total growth inhibition (TGI, the concentration at which there is no net growth) are displayed.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cell line** | **Resistance** | **AZD2014** | | **Everolimus** | |
| **GI50 (M)** | **TGI (M)** | **GI50 (M)** | **TGI (M)** |
| MCF7 parental | - | 0.138 | 0.521 | 0.056 | >10 |
| MCF7 T52 | Tamoxifen | 0.112 | 0.369 | 0.128 | >10 |
| MCF7 F100-16 | Fulvestrant | 0.035 | 0.118 | 0.184 | >10 |
| MCF7 F40-6 | Fulvestrant | 0.096 | 0.231 | 0.477 | >10 |
| HCC1428 parental | - | 0.110 | 0.324 | 0.128 | >10 |
| HCC1428 LTED | Estrogen deprivation | 0.042 | 0.198 | 0.055 | >10 |
| ZR75-1 parental | - | 0.031 | 0.110 | 0.009 | 0.101 |
| ZR75 LTED | Estrogen deprivation | 0.046 | 0.133 | 0.059 | 0.513 |

**Supplementary table 4: Activity of AZD2014 in a number of ER+ breast cancer *in vivo* models.**

Summary of anti-tumour activity in a number of ER+ breast cancer models. Tumour growth inhibition (TGI) was calculated as the reduction in treated tumour growth compared to control tumour growth at end of study and expressed as a percentage.

|  |  |  |
| --- | --- | --- |
| **Model** | **Dose/Treatment** | **TGI (%)** |
| MCF7 | AZD2014 15 mg/kg QD | 95 |
| AZD2014 20mg/kg BID 2 days on/ 5 off (measured following re-growth phase) | 70, 81 |
| Fulvestrant | 56, 40 |
| AZD2014 15 mg/kg QD + fulvestrant | 109 |
| AZD2014 20mg/kg BID 2 days on/ 5 off + fulvestrant | 104 |
| HCC1500 | AZD2014 15 mg/kg QD | 61.1 |
| Fulvestrant | 58.3 |
| AZD2014 15 mg/kg QD + fulvestrant | 99.4 |
| BR0555 | AZD2014 15 mg/kg QD | 65.4-99.8 |
| CTC174 | AZD2014 15 mg/kg QD | 84 |
| Fulvestrant | 70 |
| AZD2014 15 mg/kg QD + fulvestrant | 108 |
| HBCx3 | AZD2014 15 mg/kg QD | 65.4 |
| AZD2014 15 mg/kg QD + tamoxifen | 60.3 |