

Supplementary Table 1: Clinically relevant doses and treatment doses used in PPGL primary cultures

Drug	Treatment doses used in PPGL primary cultures	Clinically relevant doses
Everolimus	10 nM	8 nM – 59 nM (Budde et al., 2016)
Alpelisib	5 µM	2 µM – 11 µM (De Buck et al., 2014)
Sunitinib	0.5 µM	0.1 µM – 0.2 µM (Faivre et al., 2006)
Cabozantinib	5 µM	0.7 µM – 2.2 µM (Miles et al., 2016)
Dabrafenib	10 µM	8 nM – 8.9 µM (Kim et al., 2019)
Selpercatinib	5 µM	5.7 µM (Markham, 2020)
Temozolomide	100 µM	29.4 µM – 71.6 µM (Brada et al., 1999)
Niraparib	10 µM	2.4 µM – 4.4 µM (Sandhu et al., 2013)
Entinostat	1 µM	0.23 µM – 0.46 µM (Batlevi et al., 2016)
Gemcitabine	30 µM	24 µM – 32 µM (Ciccolini et al., 2016)
5-fluorouracile	20 µM	0.19 µM – 192 µM (Findlay et al., 1996)
Belzutifan	10 µM, 20 µM	3.5 µM – 4.7 µM (Choueiri et al., 2021)
Zoledronic acid	5 µM, 40 µM	1 µM – 8.3 µM (Chen et al., 2002)

- BATLEVI, C. L., KASAMON, Y., BOCIEK, R. G., LEE, P., GORE, L., COPELAND, A., SORENSEN, R., ORDENTLICH, P., CRUICKSHANK, S., KUNKEL, L., et al. 2016. ENGAGE- 501: phase II study of entinostat (SNDX-275) in relapsed and refractory Hodgkin lymphoma. *Haematologica*, 101, 968-75.
- BRADA, M., JUDSON, I., BEALE, P., MOORE, S., REIDENBERG, P., STATKEVICH, P., DUGAN, M., BATRA, V. & CUTLER, D. 1999. Phase I dose-escalation and pharmacokinetic study of temozolomide (SCH 52365) for refractory or relapsing malignancies. *Br J Cancer*, 81, 1022-30.
- BUDDE, K., ZONNENBERG, B. A., FROST, M., CHEUNG, W., URVA, S., BRECHENMACHER, T., STEIN, K., CHEN, D., KINGSWOOD, J. C. & BISSLER, J. J. 2016. Pharmacokinetics and pharmacodynamics of everolimus in patients with renal angiomyolipoma and tuberous sclerosis complex or lymphangiomyomatosis. *Br J Clin Pharmacol*, 81, 958-70.
- CHEN, T., BERENSON, J., VESCIO, R., SWIFT, R., GILCHICK, A., GOODIN, S., LORUSSO, P., MA, P., RAVERA, C., DECKERT, F., et al. 2002. Pharmacokinetics and pharmacodynamics of zoledronic acid in cancer patients with bone metastases. *J Clin Pharmacol*, 42, 1228-36.
- CHOUERI, T. K., BAUER, T. M., PAPADOPOULOS, K. P., PLIMACK, E. R., MERCHAN, J. R., MCDERMOTT, D. F., MICHAELSON, M. D., APPLEMAN, L. J., THAMAKE, S., PERINI, R. F., et al. 2021. Inhibition of hypoxia-inducible factor-2alpha in renal cell carcinoma with belzutifan: a phase 1 trial and biomarker analysis. *Nat Med*, 27, 802-805.
- CICCOLINI, J., SERDJEBI, C., PETERS, G. J. & GIOVANNETTI, E. 2016. Pharmacokinetics and pharmacogenetics of Gemcitabine as a mainstay in adult and pediatric oncology: an EORTC-PAMM perspective. *Cancer Chemother Pharmacol*, 78, 1-12.

- DE BUCK, S. S., JAKAB, A., BOEHM, M., BOOTLE, D., JURIC, D., QUADT, C. & GOGGIN, T. K. 2014. Population pharmacokinetics and pharmacodynamics of BYL719, a phosphoinositide 3-kinase antagonist, in adult patients with advanced solid malignancies. *Br J Clin Pharmacol*, 78, 543-55.
- FAIVRE, S., DELBALDO, C., VERA, K., ROBERT, C., LOZAHIC, S., LASSAU, N., BELLO, C., DEPRIMO, S., BREGA, N., MASSIMINI, G., et al. 2006. Safety, pharmacokinetic, and antitumor activity of SU11248, a novel oral multitarget tyrosine kinase inhibitor, in patients with cancer. *J Clin Oncol*, 24, 25-35.
- FINDLAY, M. P., RAYNAUD, F., CUNNINGHAM, D., IVESON, A., COLLINS, D. J. & LEACH, M. O. 1996. Measurement of plasma 5-fluorouracil by high-performance liquid chromatography with comparison of results to tissue drug levels observed using in vivo ¹⁹F magnetic resonance spectroscopy in patients on a protracted venous infusion with or without interferon-alpha. *Ann Oncol*, 7, 47-53.
- KIM, H. Y., DUONG, J. K., GONZALEZ, M., LONG, G. V., MENZIES, A. M., RIZOS, H., LIM, S. Y., LEE, J. & BODDY, A. V. 2019. Pharmacokinetic and cytokine profiles of melanoma patients with dabrafenib and trametinib-induced pyrexia. *Cancer Chemother Pharmacol*, 83, 693-704.
- MARKHAM, A. 2020. Selpercatinib: First Approval. *Drugs*, 80, 1119-1124.
- MILES, D., JUMBE, N. L., LACY, S. & NGUYEN, L. 2016. Population Pharmacokinetic Model of Cabozantinib in Patients with Medullary Thyroid Carcinoma and Its Application to an Exposure-Response Analysis. *Clin Pharmacokinet*, 55, 93-105.
- SANDHU, S. K., SCHELMAN, W. R., WILDING, G., MORENO, V., BAIRD, R. D., MIRANDA, S., HYLANDS, L., RIISNAES, R., FORSTER, M., OMLIN, A., et al. 2013. The poly(ADP-ribose) polymerase inhibitor niraparib (MK4827) in BRCA mutation carriers and patients with sporadic cancer: a phase 1 dose-escalation trial. *Lancet Oncol*, 14, 882-92.