Please read important disclosures beginning on page 3

Cytotoxicity, Scorpion Capital. Draft: Nov 20, 2026.

Our LC-MS/MS analysis of the Campos nominal concentrations in the published cytotoxicity assay demonstrate that Abivax overestimated the cytotoxicity threshold by ~150-fold (<0.38 µM vs 60 µM).

Cell-free mock assay (LC/MS-MS) reconciled with Campos 2015, Retrovirology 12:30, Figure 1c.

Abstract

Rationale

ABX464 (obefazimod; 8-chloro-N-[4-(trifluoromethoxy)phenyl]quinolin-2-amine) is a halogen-rich, low-polarity molecule whose lipophilicity, ionization, solubility and aggregation have not been disclosed experimentally, in any sources we could locate. We conducted laboratory experiments to determine the LogP using a validated method for highly lipophilic compounds and it was 6.35 (Scorpion Capital LogP, pKa, 2026). A drug with a logP of 6.35 will equilibrate into lipid membranes over water at a ratio of ~2.2 million to one, nearly insoluble in water. The intrinsic solubility we calculated from the crystalline melting point (120.5 °C, disclosed by Abivax) and our measured logP of 6.35, indicated that ABX464 was insoluble above 0.16 µM (0.000054 mg/mL). The free drug concentration is therefore limited to 0.16 µM, a concentration higher than all but lowest concentration tested in the cytotoxicity assay published by Abivax (Campos 2015). We believed that the drug concentrations in the cytotoxicity assay may have been lower than those reported since the authors state that they centrifuged the precipitate that formed when drug was added to the 500 uM master stock solution and made their serial disruptions from the supernatant.

From Campos 2015:

"…ABX464 is hydrophobic and forms aggregates when applied directly to cell cultures, which leads to some toxicity to the cells (data not shown). To avoid this problem, we prepared a soluble fraction after adding the molecule to cell culture media and elimination of aggregates by centrifugation (see Methods). The binding of ABX464 to bovine serum albumin (BSA) retains the molecule in the soluble fraction as determined by mass spectrometry. ... We also determined the concentration of ABX464 with minimal side effects on cell viability using an MTS test (Figure 1c) and cell proliferation was measured by the stable incorporation of the intracellular fluorescent dye 5-(and −6)-carboxyfluorescein diacetate succinimidyl ester (CFSE) into lymphocytes (Figure 1d). ABX464 is only toxic at doses higher than 60 µM but has no effect on cell proliferation."

Methods

We duplicated the conditions reported by Campos 2015 for the MTS test in a cell-free assay and measured the actual versus nominal drug concentrations by LC-MS/MS at each step using Tandem mass spectroscopy (Thermo Scientific TSQ Fortis Plus triple-quadrupole). We measured the assay concentrations directly and found that they contained ~19% of the concentrations plotted in the Campos cytotoxicity figure 2c. Our graphic reanalysis of the digitized points showed that both actual and nominal concentrations fell on a straight line against the MTS cytotoxicity readout (actual = 0.194 × nominal, R^2 = 0.998), with the Campos assay concentrations overestimated ~5-fold.

We sampled the solutions at each preparation step to identify where the loss occurred. Of the 254 µg in the master stock solution (1.5 ML), only 38 µg remained after centrifugation. We recovered 216 µg, or

84.9% of drug in the pellet/DMSO wash. The amount of drug in the pellet plus supernatant totaled 98% recovery. Interestingly, the drug comprised only ~1.8% of the 12 mg pellet by weight, so most of the serum components must have co-precipitated along with the drug. Collectively these data demonstrate that the overnight cold incubation followed by centrifugation was responsible for a loss of 80% to 85% of the drug in the assay and a large inflation of the safe cellular dose.

Conclusions

We conclude that the cytotoxicity assay cited concentrations that were ~5-fold higher than the actual cellular exposures, to support the claim that ABX464 was not toxic to cells above 60 μM. Abivax did not report the actual concentrations and may not have measured them. They refer to a mass spectroscopy method (quoted above) that could have been quantitative or qualitative with no associated methodology. The assay numbers graphed are the whole round numbers from the nominal dilutions, so no corrections for drug loss were apparent on the graph (figure 2c).

We reproduced their methods and demonstrated that metabolic toxicity of ABX464 on PMBC was linearly related to drug concentration and evident at every concentration tested down to a nominal concentration of 0.38 μM, where 11% cytotoxicity was still observed. There was no safe dose. The cytotoxicity claim appeared to be over-inflated by ~150-fold. This was due to an unfortunate centrifugation step that removed 85% of the drug from the master stock. solution; as well as a misinterpretation of the plotted nominal concentrations. Abivax claimed the drug was safe below 60 μM, where Campos plot 2c showed a 30% cytotoxicity readout. Our LC-MS/MS analysis shows that an actual 60 μM concentration would kill all the cells (extrapolated to 104%).

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The principal individual responsible for the research, analysis, and preparation of this report is Gurkirat Kahlon, Founder and Chief Investment Officer of Scorpion Capital LLC.