2k brief Leukemia
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High-resolution respirometry: Cancer and lymphocytes

Ex Vivo Mitochondrial Respiration Parallels Biochemical Response to Ibrutinib in CLL Cells

Subir Roy Chowdhury [1], Cheryl Peltier [1], Sen Hou [2], Amandeep Singh [1], James B. Johnston [1], Spencer B. Gibson [1,2,3], Aaron J. Marshall [1,2,3,4] and Versha Banerji [1,3,4,*]

Decreased mitochondrial respiration in chronic lymphocytic leukemia (CLL) cells from patients on ibrutinib treatment compared to pre-treatment

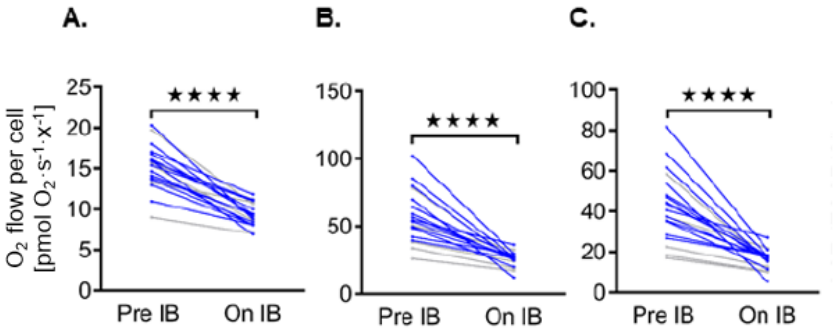

Figure 1. Ibrutinib has similar effects on mitochondrial respiration profiles in CLL patients independent of dose. The effect of ibrutinib treatment (IB) on ROUTINE respiration (**A**), ET capacity (**B**), and *E-R* reserve capacity (**C**) in primary CLL cells from patients pre-treatment and on ibrutinib treatment with low (blue) or standard (grey) dose. *N* = 14 for low dose and *N* = 5 for standard dose of ibrutinib. Values are mean ± S.D. x = 10·10^6 cells, **** $p < 0.0001$.

Patients with CLL progression while on ibrutinib treatment show increased mitochondrial respiration

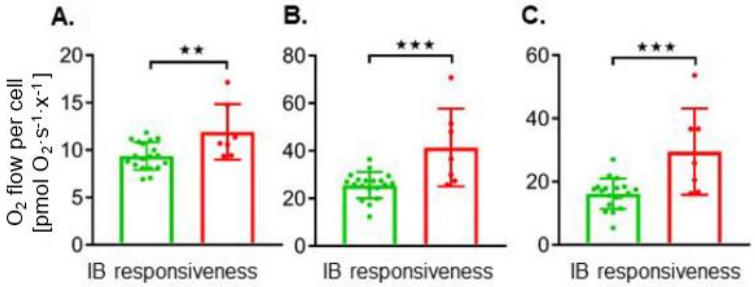

Figure 2. Patients progressed while on ibrutinib treatment have increased mitochondrial respiration profiles. ROUTINE respiration (**A**), ET capacity (**B**), and *E-R* reserve capacity (**C**) are summarized in freshly isolated CLL cells from ibrutinib-sensitive (green) and patients who have progressed on ibrutinib (red). Values are mean ± S.D., ibrutinib- sensitive, *N* = 19, and ibrutinib-progressed, *N* = 7. x = 10·10^6 cells, ** $p < 0.005$, *** $p < 0.0005$

Mitochondrial respiration of CLL cells is similarly altered regardless of ibrutinib dose in responding patients, supporting the rationale for dose reductions based on the use of a novel biomarker and mitochondrial respiration. The increase of mitochondrial respiration in patients that have progressed on therapy further supports mitochondrial respiration of CLL cells as a biomarker of active disease. Mitochondrial respiration can serve as a preclinical tool that can help identify novel compounds in the future, which can be used in parallel with standard available tools.

Reference: Chowdhury SR, Peltier C, Hou S, Singh A, Johnston JB, Gibson SB, Marshall A, Banerji V (2021) Ex vivo mitochondrial respiration parallels biochemical response to ibrutinib in CLL cells. Cancers (Basel) 13:E354.

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