Use of DiviTum®TKa assay to assess CDK4/6 inhibitor medication compliance and drug interactions.

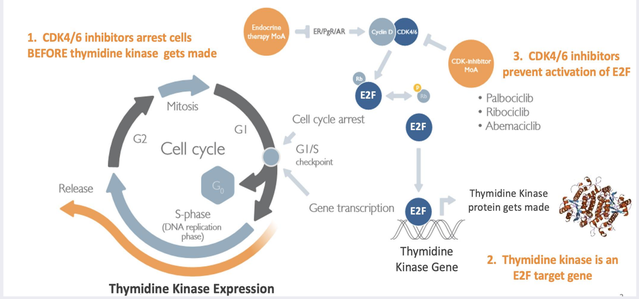
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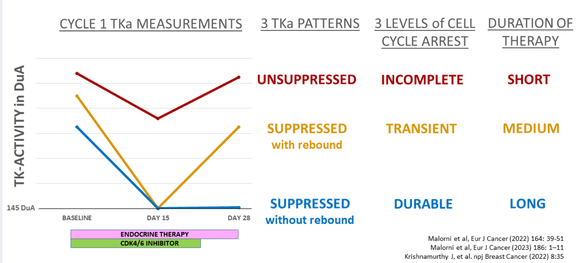
BACKGROUND

- Divitum TKa assay measures thymidine kinase activity (TKa), a marker of cell proliferation, in the serum.
- Divitum TKa assay was FDA approved in July 2022 for disease monitoring in breast cancer.
- CDK4/6 inhibitors have several known drug-drug interactions which can affect their concentration, efficacy, or safety profile.
- In this study, we assessed if TKa values on C1D15 of CDK4/6 inhibitor therapy could identify low compliance or drug interactions and if counseling or adjusting medications could restore optimal TKa levels.

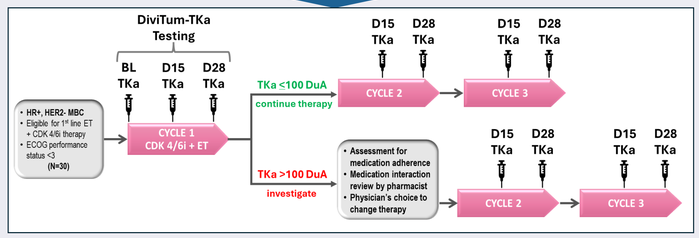
Thymidine Kinase activity as a pharmacodynamic biomarker for CDK4/6 inhibition



Cycle 1 TKa dynamics can predict tumor response and patient benefit to CDK4/6i based therapy



METHODS



- Single institution pilot study of patients with ER+ metastatic breast cancer on first line CDK4/6i and endocrine therapy.
- Participants with a sustained TKa level (>100 DuA) were assessed for medication compliance and drug-drug interactions by the study team.
- Participants were counseled on medication compliance and/or medications were adjusted as needed by treating oncologist.

RESULTS

- 30 patients were enrolled 1/2024-5/2025
- All participants had at least 3 consecutive TKa levels

	N	%
Participants	30	
Age	Median 64	
White	23	76.7
Black	4	13.3
Asian	1	3.0
Unknown	2	7.0
Visceral Disease	7	23.3
Non-visceral	23	76.7
Ribociclib	17	56.7
Abemaciclib	11	36.7
Palbociclib	2	6.6

	N	mPFS
TKa consistently suppressed (DuA <100)	25	Not reached
TKa elevated then suppressed	3	Not reached
TKa consistently elevated (DuA>100)	2	2.5 mo

Examples of TKa Dynamics

Figure 1: Medication Compliance

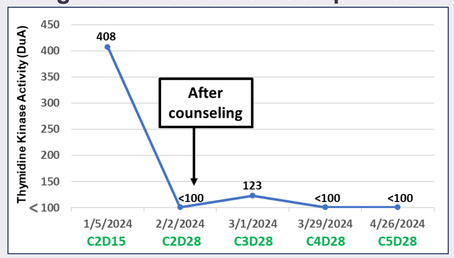


Fig 1: TKa levels elevated on C2D15. Participant was found to be taking abemaciclib once a day. After counseling, started taking it twice a day. TKa levels decreased. SD.

Figure 2: CDK4/6i Therapy Resistance

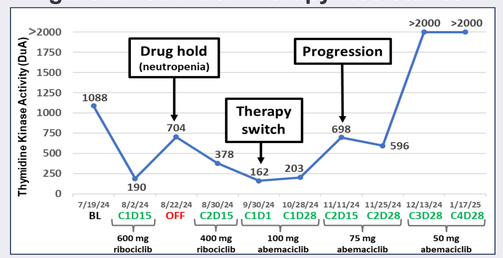


Fig 2: TKa levels never suppressed to <100 DuA while on therapy. Switched to abemaciclib which was dose reduced in cycle 1 due to neutropenia. Elevated TKa in Nov with POD on scan.

Figure 3: Early progression

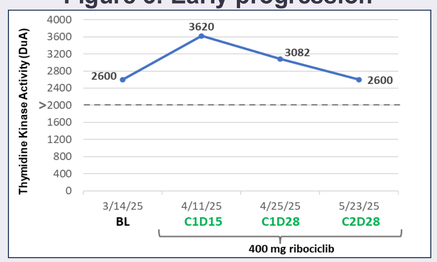


Fig 3: Pt with bone only disease and high BL TKa that remained persistently elevated on therapy. No compliance or DDI issues identified. POD at 3 mo.

Figure 4: Drug-drug Interaction

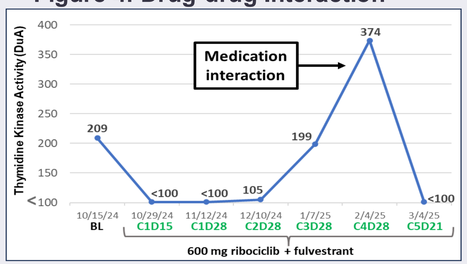


Fig 4: TKa levels suppressed to <100 DuA on therapy by C1D15. TKa rises rapidly in Feb. Found to be on Bactrim. TKa levels re-suppressed when pt is off antibiotic. SD.

- The Divitum TKa assay can be a useful tool in monitoring adherence and drug-drug interactions in the clinic.
- Suboptimal TKa response can identify issues that could be addressed with counseling and concomitant medication review.
- Persistently elevated TKa levels early on-treatment predict short PFS, whereas suppression of TKa levels is associated with prolonged PFS.

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