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Note d'application

Advantages of Using MaxPeak™ HPS™ Technology for the Analysis of Targeted Cancer Growth Inhibitor Therapies

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This is an Application Brief and does not contain a detailed Experimental section.

Abstract

Non-specific binding of analytes to material surfaces is an inherent characteristic of conventional chromatographic columns and systems. This phenomenon leads to reduced sensitivity and sometimes poor peak shape. The MaxPeak Premier Technology provides a solution without the need for strong mobile phase additives, chelators, or lengthy passivation protocols. A panel of targeted cancer growth inhibitor therapies was utilized to demonstrate the chromatographic benefits provided when using columns and systems equipped with MaxPeak Premier Technology.

Benefits

- MaxPeak Premier Technology provides improved chromatographic peak performance for targeted cancer growth inhibitor therapies without the need for strong mobile phase additives, chelators, or lengthy passivation protocols

- The chromatographic sensitivity of cancer growth inhibitors is improved when using materials equipped with MaxPeak Premier Technology

Introduction

Targeted cancer therapies are drugs or other substances which affect chemical factors in the body that trigger cancer cells to divide and grow. These compounds act by lowering the levels of growth factors in the body, impeding growth receptors on the cancer cell surface, or blocking the signal cascade inside the cell that begins after triggering of the cell receptor. Classes of growth inhibitors include tyrosine, kinase inhibitors, proteosome inhibitors, mTOR inhibitors, PI3K inhibitors, histone deacetylase inhibitors, hedgehog pathway blockers, and BRAF/MEK inhibitors. Individual therapies are prescribed to patients according to the type of cancer, stage, and growth factor targeted for inhibition.[1]

When analyzing these therapies by chromatography, mobile phase ion-pairing agents and chelating agents, such as 0.1% trifluoracetic acid (TFA), are routinely added to improve peak shape. Unfortunately, use of these reagents requires unavoidable column and system passivation steps to establish and stabilize the protective barrier between the analyte and material surfaces. Not only does surface passivation gradually decline over time, it can inherently result in irreversible alterations in column selectivity, reduced chromatographic precision, high background interference, and/or low sensitivity in both ultraviolet (UV) and liquid chromatography-mass spectrometry (LC-MS) applications.[2,3]

The objective of the work shown here is to demonstrate the chromatographic performance of the MaxPeak Premier Technology, a material specifically designed to provide exceptional chromatographic performance. A panel of cancer growth inhibitor therapies were used as representative analytes to compare sensitivity (peak height) and peak performance (tailing and peak width at 5σ) with conventional chromatographic materials.

Experimental

LC system 1:	ACQUITY™ Arc™ System with Quaternary Solvent Manager (rQSM), Sample Manager (rFTN), ACQUITY Arc Column Manager (rCM), Empower™ 3 Chromatography Software
LC system 2:	Arc Premier System with Quaternary Solvent Manager (rQSM), Arc Premier Sample Manager (rFTN), Empower 3 Chromatography Software
Detection:	ACQUITY Photo Diode Array Detector (PDA), UV 275 nm
Column(s):	XBridge™ Premier BEH™ Shield $RP_{18,}$ 2.5µm Column, 4.6 x 150 mm, p/n: 186009923 XBridge BEH Shield RP_{18}, XP, 2.5 µm Column, 4.6 x 150 mm, p/n: 186006717
Column temp.:	40 °C
Sample temp.:	20 °C
Injection volume:	1 µl
Flow rate:	1.3 mL/min
Mobile phase A:	10 mM Ammonium formate pH 4.0
Mobile phase B:	Acetonitrile
Gradient:	2–95% mobile phase B over ten minutes,

two-minute hold at 95% mobile phase B,
then return to 2% mobile phase B

Results and Discussion

Individual mixtures of cancer growth inhibitor therapies (Figure 1): Panobinostat, Imatinib, Sunitinib, Bortezomib, Idelalisib, Visomdegib, Vemurafenib, and Everolimus, were prepared individually by dissolving approximately 0.5 mg in 2 mL of acetonitrile. LC instruments were flushed with 100% IPA, water, then mobile phase.

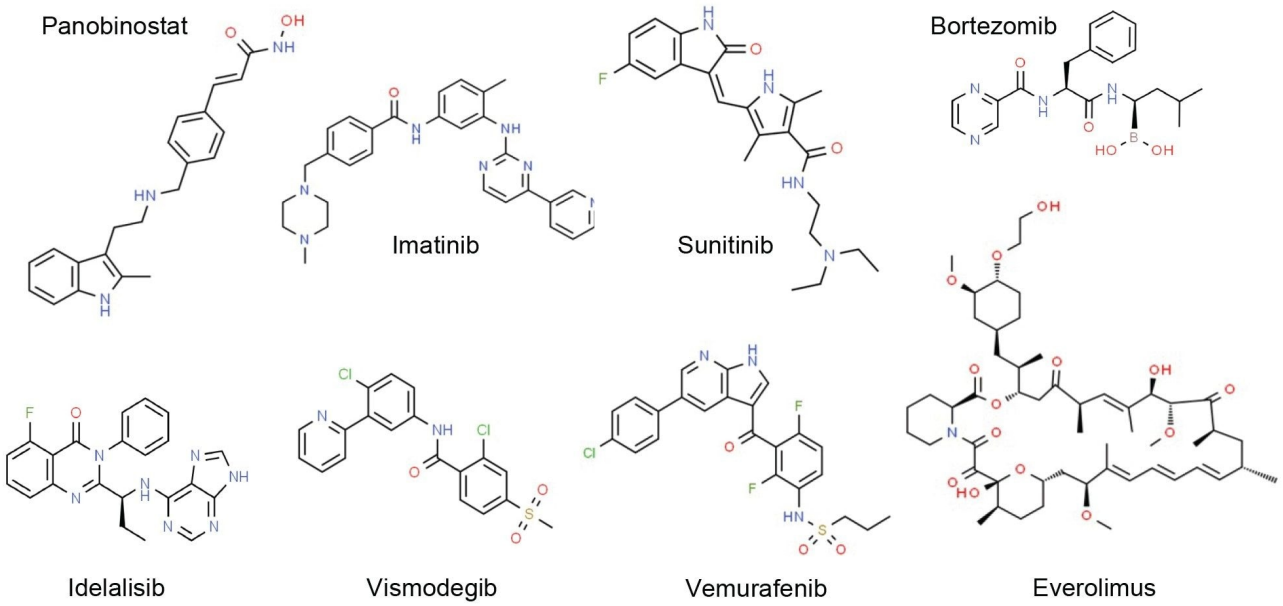

Figure 1. Panel of the cancer growth inhibitor targeted therapies used in this study.[4]

The chromatographic method separated all eight targeted therapies in the panel (Figure 2). A 2.7-fold increase in sensitivity (peak height) was observed with the addition of the MaxPeak Premier Column when results are compared to those obtained with conventional materials (*i.e.*, BEH Shield RP_{18} XP and ACQUITY Arc System). An even greater increase in response (peak height) was observed, at between 2.0 and 9.0 fold, compared to

conventional materials (Table 1, Figure 3) when the MaxPeak Premier technology was employed in both the column and system (*i.e.* Premier BEH Shield System). Similarly, peak tailing and peak width at $5\sigma^5$ improved for all analytes after the addition of the MaxPeak Premier Technology (Figure 4 and 5). Painobinostat was the most affected analyte in the panel, with a decrease in tailing of 3.4-fold and peak width improvement at 5σ of 5.6-fold, when compared to analysis with the conventional system and column.

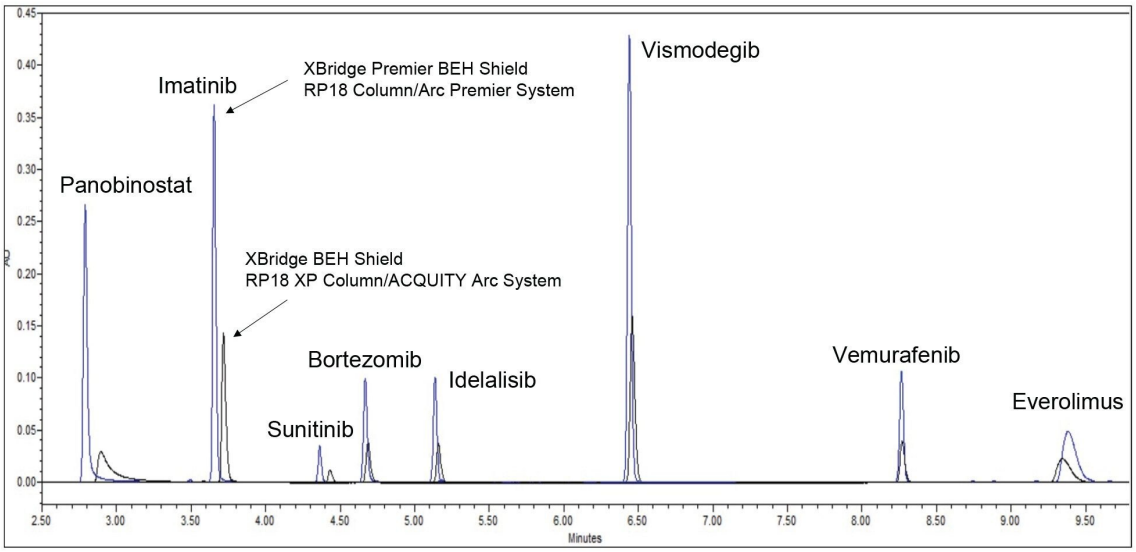

Figure 2. Chromatographic overlay of the panel of targeted cancer growth inhibitor therapies analyzed using the (black) XBridge BEH Shield RP_{18} XP Column/ACQUITY Arc System and the (blue) XBridge Premier BEH Shield RP_{18} Column/Arc Premier System.

Cancer growth inhibitor	XBridge Premier BEH Shield RP18 Column/ACQUITY Arc System	XBridge Premier BEH Shield RP18 Column/Arc Premier System
Panobinostat	2.7	9.0
Imatinib	1.2	2.5
Sunitinib	1.2	2.8
Bortezomib	1.2	2.6
Idelalisib	1.2	2.7
Vismodegib	1.2	2.7
Vemurafenib	1.2	2.7
Everolimus	1.0	2.1

Table 1. Fold increase in sensitivity with the XBridge Premier BEH Shield RP_{18} Column and/or the Arc Premier System compared to the XBridge BEH Shield RP_{18} XP Column ACQUITY Arc System.

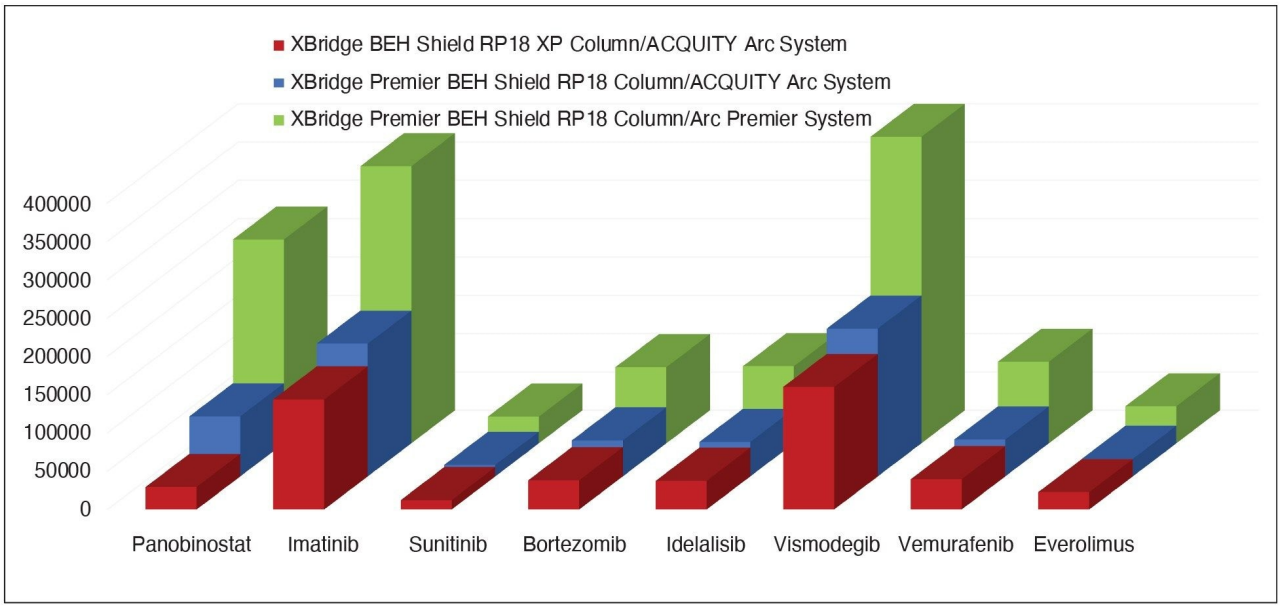

Figure 3. Peak height with the (red) XBridge BEH Shield RP_{18} XP Column/ACQUITY Arc System, (blue) XBridge Premier BEH Shield RP_{18} Column/ACQUITY Arc System, and (green) XBridge Premier BEH Shield RP_{18} Column/Arc Premier System.

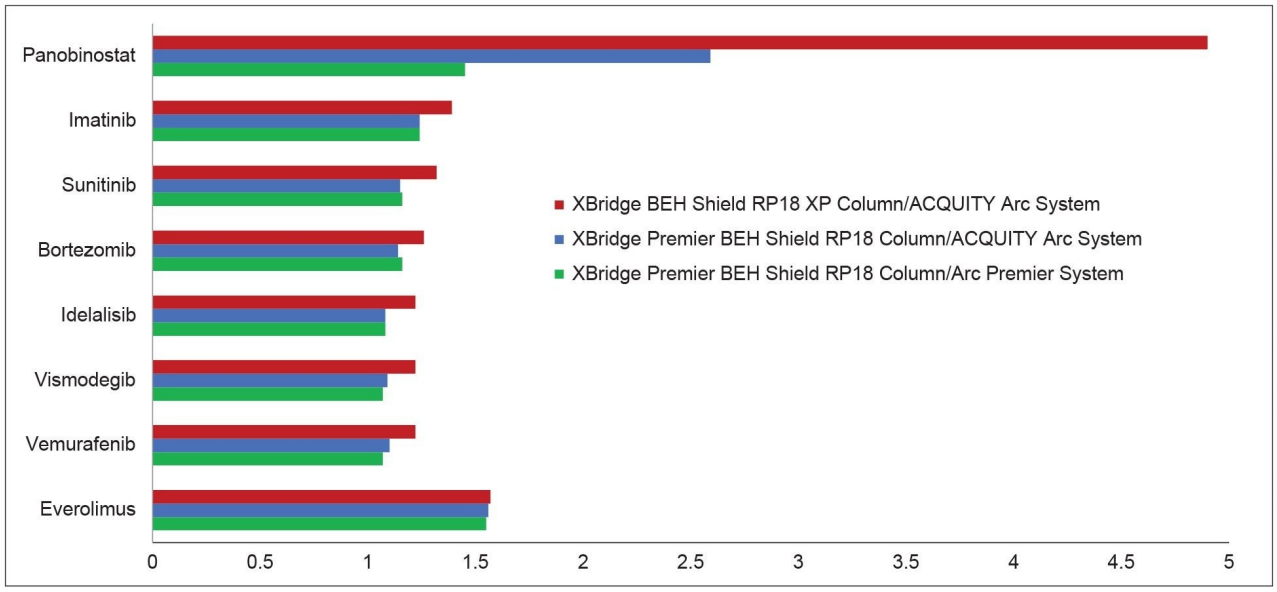

Figure 4. USP peak tailing with the (red) XBridge BEH Shield RP_{18} XP Column/ACQUITY Arc System, (blue) XBridge Premier BEH Shield RP_{18} Column/ACQUITY Arc System, and (green) XBridge Premier BEH Shield RP_{18} Column/Arc Premier System.

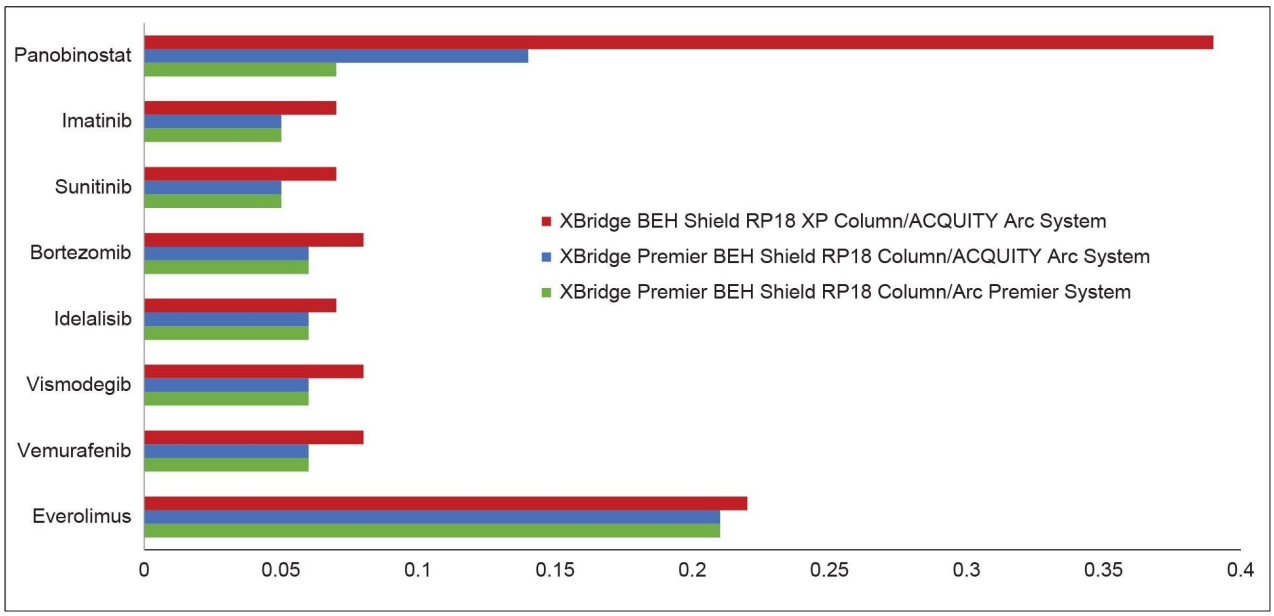

Figure 5. Peak width at 5σ with the (red) XBridge BEH Shield RP_{18} XP Column/ACQUITY Arc System, (blue) XBridge Premier BEH Shield RP_{18} Column/ACQUITY Arc System, and (green) XBridge Premier BEH Shield RP_{18} Column/Arc Premier System.

Conclusion

The data exhibited chromatographic sensitivity and peak performance improvements when employing MaxPeak Premier Technology for the analysis of targeted cancer growth inhibitor therapies. With this technology, a gain in performance was achieved without the use of strong ion-pairing agents or lengthy method passivation protocols. Although some analytes in our panel demonstrated a higher susceptibility towards non-specific surface binding, there was no decrease in chromatographic performance observed with MaxPeak Premier Technology across the panel. This suggests that deployment of the MaxPeak Premier Technology during future method development and quality testing of this class of drug therapies would potentially reduce the risk for analyte loss and peak performance degradation due to non-specific, chromatographic surface interactions.

References

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