Lateral Flow Immunoassays for Point-of-Care Dose Monitoring of Antibody Therapeutics

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ABSTRACT

Monoclonal antibodies (mAb) are promising therapies increasingly used to treat serious diseases such as cancer, rheumatoid arthritis, Crohn's disease, and multiple sclerosis. However, current dosing strategies for these expensive mAb drugs are not customized for each patient, and there is growing evidence of large inter-patient variations in circulating mAb drug levels. Furthermore, multiple studies with different mAb drugs have shown that patients with low circulating drug levels have poorer therapeutic outcomes; these patients may benefit from more frequent dosing or higher doses. On the other hand, patients whose mAb drug levels are well above the range required for optimal clinical benefit could receive reduced doses or have subsequent treatments delayed, which would mitigate side effects without affecting outcomes, and, importantly, reduce healthcare costs. Physicians currently lack tools for monitoring mAb drug levels in their patients in real time, and are thus unable to identify treatment failures in patients with low mAb drug levels or prevent excessive dosing in other patients.

To address this need, Abreos Biosciences has developed lateral flow immunoassay (LFA) devices that measure mAb drug levels in blood and can be used to guide dosing of these therapeutic agents. Unlike other blood-based assays, key advantages of Abreos Biosciences' LFA devices are that they do not require a lab, can be executed at various point-of-care settings, and yield results that are immediately implementable by treating physicians for real-time precision dosing. Our devices utilize proprietary Veritope™ reagents as a surrogate ligand to specifically capture active mAb drug in biological samples. Paired with a digital reader, these LFA enable quantitative readouts of mAb drug levels from a single drop of blood in less than 10 minutes. By leveraging the simplicity, speed, low cost, and convenience of LFA, Veritope™-based devices will enable physicians to guide accurate dosing of their patients for improved clinical outcomes, reduced side effects, and lower healthcare costs.

BACKGROUND

Limitations of Standard Dosing Practice

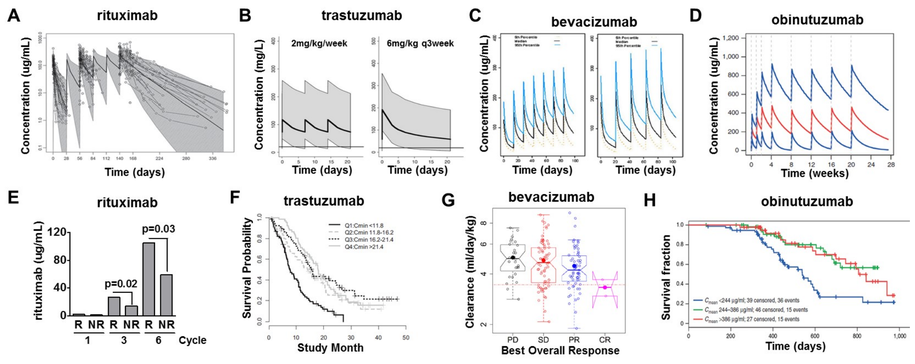

FIGURE 1. Actual drug levels vary enormously in people given the same standard dose, which is associated with poorer clinical outcomes. (A-D) Examples of actual interpatient or predicted pharmacokinetic variation of monoclonal antibodies (mAb) [1-4]. (E-H) mAb drug levels are associated with clinical response [1,5,6,4]. Such variations in mAb drug levels can be explained by several patient-specific factors, including demographics, tumor burden, non-specific mAb clearance and degradation, immunogenicity, and other variables associated with the simultaneous administration of other treatments.

TECHNOLOGY PLATFORM

Veritope™ Reagents for Biologic Drug Detection

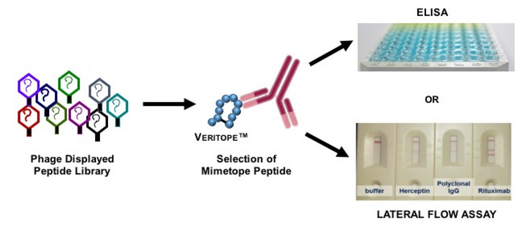

FIGURE 2. Veritopes are robust mimetope peptides that specifically detect a given biologic or biosimilar drug by mimicking the natural ligand of the molecule. Phage display libraries are used to identify peptides that bind to the mAb of interest. Selected peptides are synthesized and validated by ELISA. Validated peptides can be implemented in lab-based immunoassays such as ELISA or lab-free devices such as lateral flow assay (LFA).

TECHNOLOGY APPLICATIONS

LFA for Biologic Drug Authentication at Point-of-Care

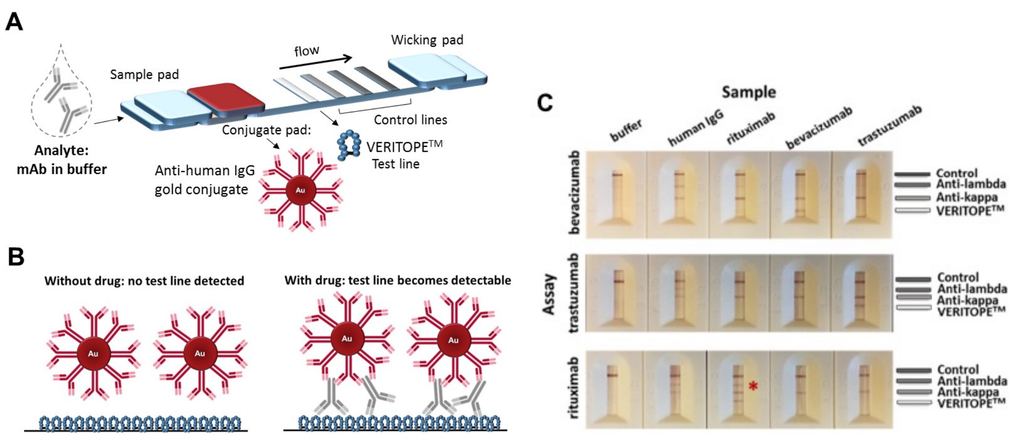

FIGURE 3. LFA devices for mAb detection using Veritope™ peptides. (A-B) Schematic of LFA design based on sandwich assay format. (C) Working prototypes for detection of reconstituted suspensions of rituximab, bevacizumab, and trastuzumab from the infusion pharmacy. Prototypes were 100% accurate for detection of the correct mAb. Quantitative versions are in development.

LFA for Personalized Dose Monitoring of Biologic Drugs at Point-of-Care

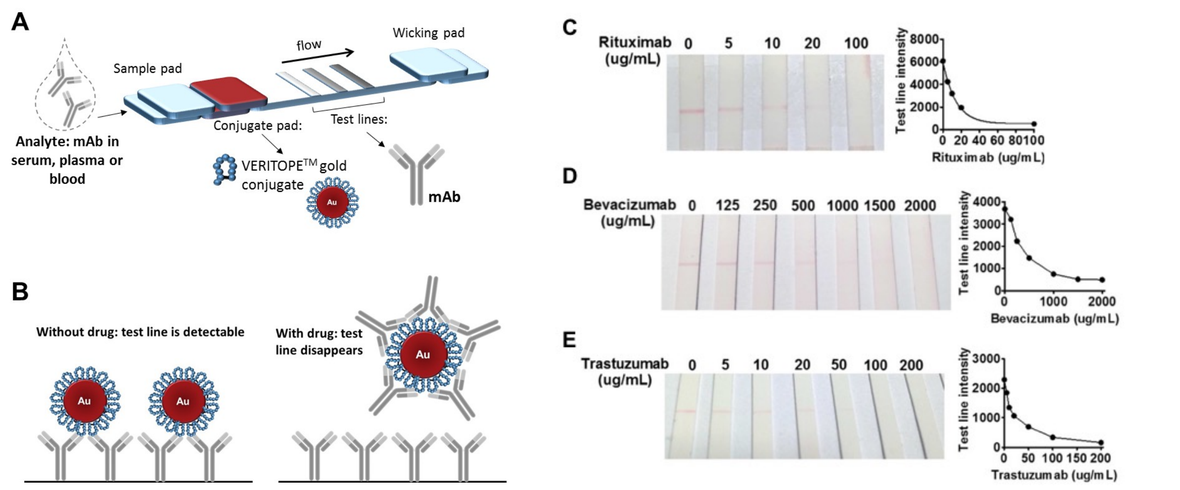

FIGURE 4. Competitive Veritope™ LFA for mAb drug monitoring in biologic samples. (A-B) Schematic of LFA design based on competitive assay format. (C-E) Feasibility study of competitive Veritope™ LFA for mAb drug detection in serum. mAb was spiked in serum at relevant *in vivo* (therapeutic) concentrations and applied to strips. Test line intensity was measured with an Axxin AX-2X digital reader.

Pipeline of Veritope™ Reagents

mAb drug	Drug maker	Cellular target	Status
Rituximab (Rituxan)	Roche	CD20	Validated
Trastuzumab (Herceptin)	Roche	HER2	Validated
Bevacizumab (Avastin)	Roche	VEGF	Validated
Alemtuzumab (Campath)	Genzyme	CD52	Validated
Obinutuzumab (Gazyva)	Roche	CD20	Validated
Natalizumab (Tysabri)	Biogen Idec	VLA-4	Validated
Infliximab (Remicade)	Johnson & Johnson	TNF-alpha	In progress
Adalimumab (Humira)	AbbVie	TNF-alpha	In progress
Nivolumab (Opdivo)	Bristol-Myers Squibb	PD-1	In progress
Pembrolizumab (Keytruda)	Merck & Co.	PD-1	In progress
Ipilimumab (Yervoy)	Bristol-Myers Squibb	CLTA4	In progress
Cetuximab (Erbitux)	Eli Lilly	EGFR	In progress

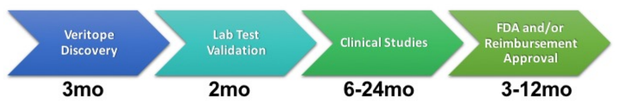

Figure 5. Veritope™ reagents in development at Abreos Biosciences and final product development timeline. The use of mimetope peptides for detection of antibody therapeutics in biological samples is covered by patent number US 9,250,233 B2 [7], and Abreos Biosciences, Inc. has an exclusive license to this patent from the University of California, San Diego.

Quantitative Lab-Free Reader Devices for LFA

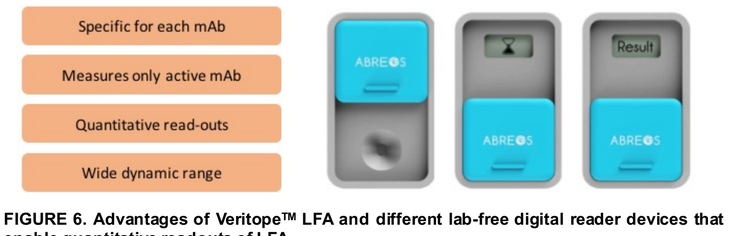

FIGURE 6. Advantages of Veritope™ LFA and different lab-free digital reader devices that enable quantitative readouts of LFA.

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SUMMARY

- Abreos Biosciences is a diagnostics company developing dose monitoring assays for biologic drugs.
- Precision dosing of these expensive medications can improve outcomes at lower costs, but assays to measure the circulating level of a given drug in a treated patient's blood are not widely available to clinicians.
- Our core technology is the Veritope™ platform. Veritopes™ are peptide mimics of the natural ligand bound by a monoclonal antibody or other biologic drug.
- Veritopes™ are ideal for traditional sandwich immunoassays in a clinical lab setting as well as lateral flow assays for point-of-care or point-of-patient testing.
- Veritopes™ are easier to produce, cheaper, and more robust than traditional protein reagents.
- Abreos has completed prototype assays and devices for several monoclonal antibodies including rituximab and trastuzumab and has identified Veritope™ reagents for several of the top 10 monoclonal antibodies on the market.
- We are actively seeking strategic partnerships with biologic drug developers and distributors, health care systems and payers, and government agencies.

ADDITIONAL INFORMATION

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Financial Disclosures:
Dr. Bradley Messmer is Founder and CEO of Abreos Biosciences and along with Dr. Dina Uzri, Dr. Jessie-F. Fecteau, Dr. Laura Ruff, and Neil Senturia receive stock compensations from Abreos Biosciences, Inc.

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