Latest Results from the On-going Clinical Studies Utilizing the Novel Fluorescent Tracer Agent MB-102 for Transdermal Glomerular Filtration Rate Measurement

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Background / Purpose

Measurement of glomerular filtration rate (GFR) is widely accepted as the most reliable measure of renal function. The optimum measure of GFR is by the use of exogenous tracer agents. However this methodology requires several blood draws as a function of time and subsequent laboratory analysis to measure tracer agent concentration in each blood draw. Hence, these exogenous tracer agents are not amenable to the bedside for point-of-care application, and in practice they are mainly employed for research purposes. To overcome the deficiencies of these research GFR tracer agents, we have developed MB-102, a transdermally detectable exogenous fluorescent agent which combines the optimum measurement of an exogenous tracer agent with point-of-care bedside utility.

Objectives

- Compare plasma pharmacokinetics of MB-102 with iohexol to demonstrate MB-102 is a GFR tracer agent in humans with both normal and impaired renal function.
- Measure the percent of administered dose of MB-102 excreted from the renal system.
- Compare the transdermal-measured fluorescence clearance with the plasma-measured clearance of MB-102 using a prototype noninvasive fluorescence detection device.
- Monitor the safety and tolerance of MB-102 in humans.

Methods

Blood samples were taken from120 subjects with eGFR ranging from normal to Stage 4 CKD values, most over a period of 12 hours post simultaneous administration of MB-102 and iohexol. Urine was collected post-dose to assess percent administered dose excretion. A noninvasive detection device placed on the sternum measured the transdermal fluorescence from MB-102 over the 12 hour post-dose time period. All three techniques were performed simultaneously.

Results: Plasma Pharmacokinetics

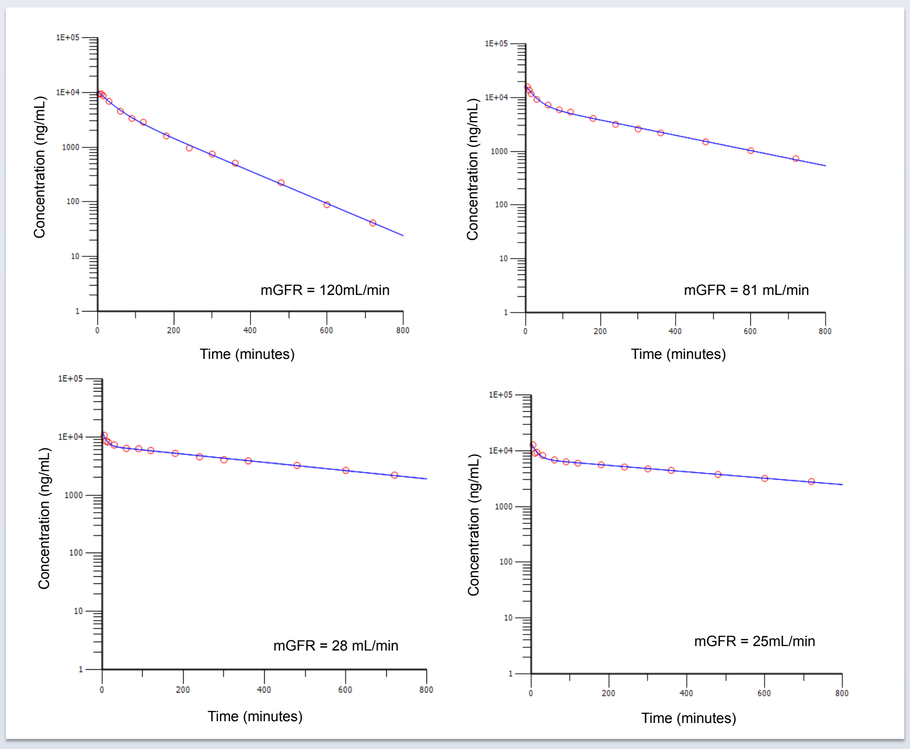

Figure 1: Concentration of MB-102 in plasma over time for subjects with normal to Stage 4 CKD renal function.
Red circles are measured concentrations, blue line is two-compartment pharmacokinetic fit.

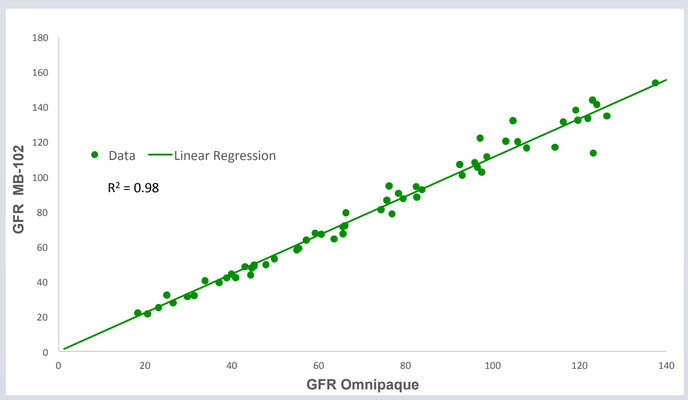

Figure 2: Correlation of MB-102 plasma-derived GFR with Omnipaque plasma-derived GFR.
The regression line yields a high correlation over the entire range of GFR values, thus we conclude that MB-102 is a GFR tracer agent for subjects with normal and impaired kidney function.

Results: Fluorescence Pharmacokinetics

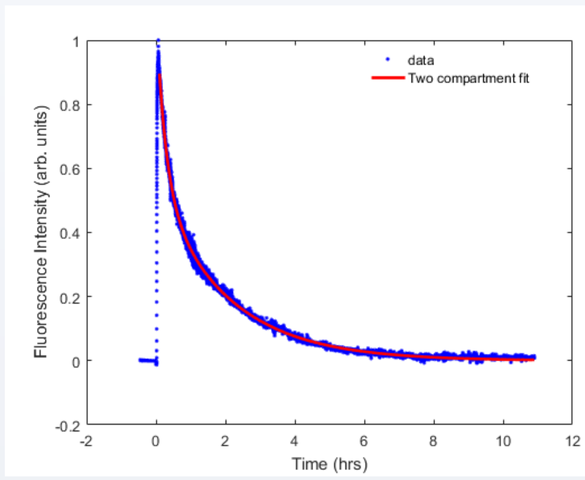

Figure 3: Transdermal fluorescence from MB-102 measured at sternum in Subject 11. Blue circles are measured values, the red line is a fit to the pharmacokinetic model. The terminal (second compartment) half-life is approximately 84 minutes.

Figure 4: Transdermal Fluorescence Pharmacokinetics Correlates with Plasma Pharmacokinetics Over Range of GFR.
Plasma concentration versus fluorescence intensity at the same time points in the renal excretion phase yield an almost perfect correlation over the entire range of GFR values.

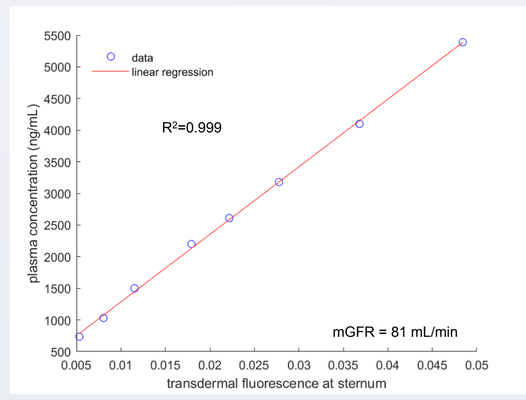

Figure 5: nGFR vs. fluorescence clearance rate (inverse of measured transdermal time constant) for 45 subjects of study (Dorshow-Debreczeny plot).
The data in Figure 5 was used to construct version 1 of our correlation algorithm between fluorescence time constant and plasma GFR, similar to the work of Rabito et al. (2010).

Summary of Results

The GFR measured from the MB-102 plasma pharmacokinetics was highly correlated with the GFR measured from iohexol over the entire measured range of GFR values (r^2=0.98). The time-dependence of the transdermal fluorescence from MB-102 monitored by our fluorescence detection device was highly correlated with that of the plasma (see Figure 4). MB-102 was completely cleared by 12 hours when GFR was >60 mL/min/1.73 m^2. No significant adverse events were reported.

Conclusion

Point-of-care clinically amenable measured GFR for a range of kidney function from normal to Stage 4 CKD is demonstrated using transdermal fluorescence detection of the novel fluorescence tracer agent MB-102.

References

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Dorshow, R. B., et al., 2015. Initial clinical trial results of a real-time point-of-care glomerular filtration rate measurement utilizing a novel fluorescent tracer agent. J Am Soc Nephrol 26, 259A.

Rabito, C. A., et al., 2010. Accurate, fast, and convenient measurement of glomerular filtration rate in potential renal transplant donors. Transplantation 90, 510-517.

Definitions:

eGFR: Estimated GFR using CKD-EPI equation.
mGFR: Measured GFR using plasma pharmacokinetic data (MB-102)
nGFR: mGFR normalized to body surface area