Absence of Interactions Between AST-120 (Spherical Carbon Adsorbent), a Novel Oral Adsorbent, and Concomitant Medications: Azathioprine and CiproXR®

Jonathan Willmer[1], Keith Anderson[2], Scott Proksch[2], Caroline LaPlaca[2], M. Scott Harris[2]

Aim:

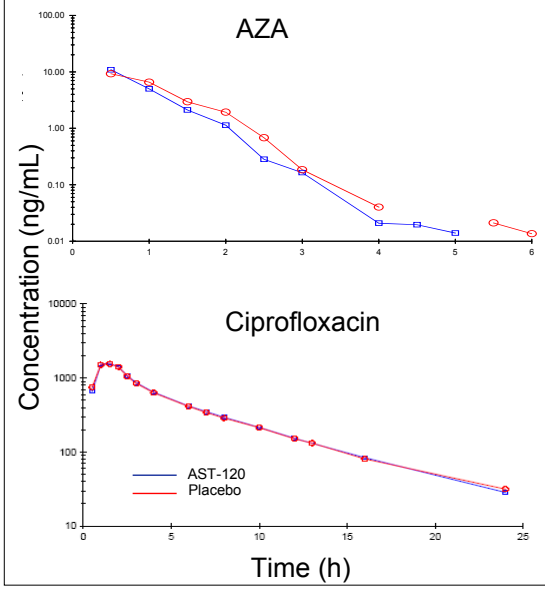
This investigation was intended to evaluate the potential for drug-drug interactions between AST-120 and medications commonly used in the treatment of IBD.

Background:

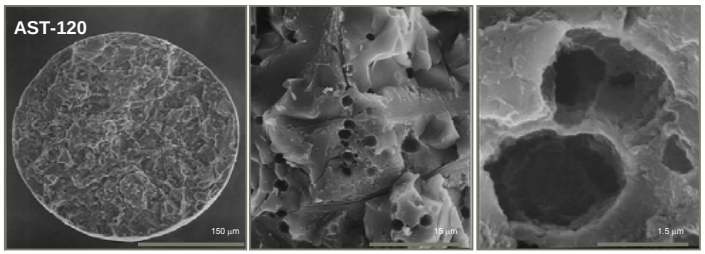
- AST-120 is an orally-administered, non-absorbed, carbonaceous microsphere. Its extensive pore structure confers high specific surface area (>9600 m^2/ 6g daily dose).
- AST-120 selectively adsorbs a broad range of pro-inflammatory mediators that have been implicated in IBD disorders.

Methods:

- 60 healthy volunteers were randomized between Cipro XR® (CFXR) or Azathioprine (AZA); “active treatment”.
- Treatment groups were divided into 15-subject cohorts randomly assigned to be treated with a single dose of active treatment followed by either 2 g AST-120 TID or 2g placebo TID in a crossover design.
- The initial dose of placebo or AST-120 was given 30 minutes after the active treatment dose, then followed at regular intervals during waking hours.
- Blood samples were analyzed for CFXR or AZA in plasma using validated LC/MS/MS bioanalytical methods.



Compound	AUC_{last} (ng*hr/mL)	AUC_{∞} (ng*hr/mL)	C_{max} (ng/mL)
AST + AZA	9.64 ± 4.52	10.30 ± 4.74	11.86 ± 6.86
AZA + Placebo	10.64 ± 4.82	11.45 ± 4.72	11.22 ± 6.45
Mean Ratio	88.4 %	89.8 %	101.4 %
90% CI	80 - 97 %	81 - 99 %	85 - 121 %
AST + CFXR	7602.29 ± 2325.61	7956.50 ± 2391.46	1722.50 ± 414.01
AST + Placebo	7557.85 ± 2467.90	7918.32 ± 2537.09	1762.69 ± 594.22
Mean Ratio	101.9 %	101.8 %	100.6 %
90% CI	92 – 112 %	92 – 112 %	91 -111 %



Discussion:

These results confirm that concomitant administration of AST-120 with CFXR or AZA has no impact on the pharmacokinetics or bioavailability of these compounds according to standard bioequivalence guidelines. The maximal binding kinetics for compounds to AST-120 typically ranges from 4-6 hr *in vitro*, which represent a slower rate constant than that typically represented by absorption of compounds in the upper GI tract. This supports the hypothesis that the adsorption of pro-inflammatory mediators to AST-120 occurs predominantly in the lower GI tract.

[1]Cantest, Vancouver, Canada [2]Ocera Therapeutics Inc., San Diego, CA