A proof-of-concept study to evaluate the efficacy and safety of BTI320 on post-prandial hyperglycemia in high risk Chinese subjects with pre-diabetes

Andrea O.Y. Luk, Benny C.Y. Zee, Marc Chong, Risa Ozaki, Carl W. Rausch, Michael H.M. Chan, Ronald C.W. Ma, Alice P.S. Kong, Francis C.C. Chow, Juliana C.N. Chan

Background

Galactomannan(s) are the active ingredient in natural gum and have been shown to reduce post-prandial blood glucose by delaying intestinal absorption of carbohydrates and slowing down gastric emptying. BTI320 is a proprietary combination of fractionated mannans administered in the form of a chewable tablet.

Objective

In this proof-of-concept study, we examined the glycemic efficacy, tolerability and safety of 16 weeks' intervention with BTI320 compared with placebo in high risk Chinese adults with pre-diabetes.

Methods

We undertook a randomized, double-blind, placebo-controlled, parallel arm study with the first subject enrolled on 30 March 2015 and the last subject completed the study on 19 February 2016. The study was conducted at the Diabetes and Endocrine Centre of the Chinese University of Hong Kong at the Prince of Wales Hospital, Hong Kong. The study is registered at www.clinicaltrials.gov, reference number NCT02358668.

60 Chinese adults aged 18-70 years with either impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or HbA1c 5.7-6.4% were randomly assigned in 2:2:1 ratio to either BTI320 8 grams (high dose), BTI320 4 grams (low dose) or matching-placebo three times daily before each main meal for 16 weeks.

The primary endpoint was change in serum fructosamine level in subjects treated with BTI320 compared with placebo from baseline to week 4. Indices of glycemic variability based on continuous glucose monitoring (CGM) were explored in secondary analyses. Efficacy analyses were performed in the intention-to-treat population which consisted of subjects who have received at least one dose of the assigned treatment.

Results

Of 60 subjects randomized, 2 subjects on low dose BTI320 withdrew from the study due to adverse events and 1 subject on high dose BTI320 withdrew consent for non-medical reasons. The mean age of the cohort was 56.4±9.1 years and 46.7% were male. At baseline, glycemic indices were comparable among the three intervention arms (Table 1).

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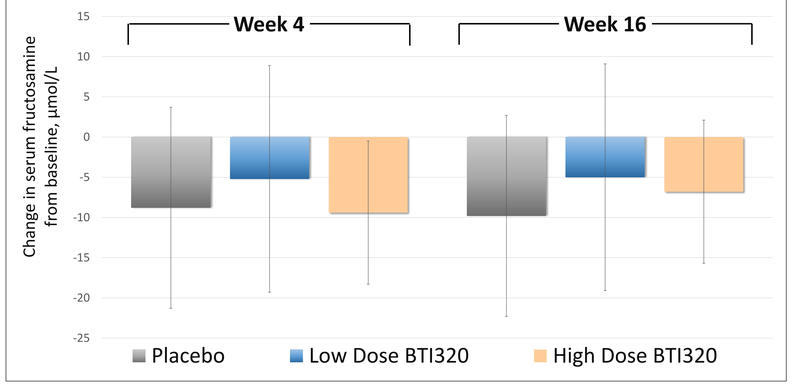
Table 1: Baseline clinical characteristics of 60 randomized subjects

	Placebo	Low Dose BTI320	High Dose BTI320
Number	12	24	24
Body weight, kg	63.9±20.0	74.2±16.9	71.0±16.2
BMI, kg/m^2	25.1±4.3	28.0±5.8	26.9±4.4
Fructosamine, µmol/L	278.9±22.0	268.5±18.3	272.2±20.2
HbA1c, %	6.1±0.3	6.0±0.3	6.0±0.3
IFG, % (n)	0.0 (0)	12.5 (3)	4.2 (1)
IGT, % (n)	41.7 (5)	41.7 (10)	33.3 (8)
Both IFG/IGT, % (n)	33.3 (4)	16.7 (4)	29.2 (7)
NGT and HbA1c 5.7-6.4%	25.0 (3)	29.2 (7)	33.3 (8)

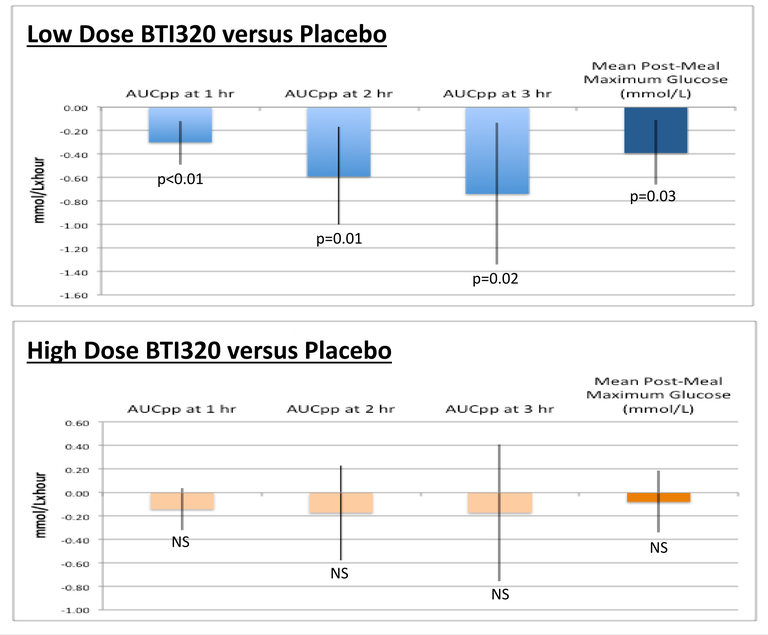
The changes in serum fructosamine levels from baseline to 4 weeks were -5.2, -9.4 and -8.8µmol/L in subjects receiving low dose BTI320, high dose BTI320 and placebo, respectively (Figure 1). The estimated mean differences in change in fructosamine levels were not significant for comparison between intervention with BTI320 and placebo. At 16 weeks, there were no differences in changes in fructosamine and HbA1c from baseline between active and placebo arms.

Figure 1: Changes in serum fructosamine levels from baseline



Parameters of post-prandial glucose excursion were calculated based on data from CGM. Using random effect models adjusted for variability by meals, treatment with low dose BTI 320 but not high dose BTI320 was associated with reduction in post-prandial incremental area-under-curve (AUC) and mean post-meal maximum glucose (MPMG) compared with placebo (Figure 2). Body weight was reduced in low dose BTI320 group with mean change in weight -1.7 kg (95% CI -3.2, -0.1) kg relative to placebo. More subjects receiving BTI320 reported abdominal distension and increased flatulence but there were no reports of hypoglycemia.

Figure 2: Changes in post-prandial glucose from baseline between BTI320 intervention and placebo



Conclusion

Low dose BTI320 (4 grams three times daily) attenuated post-prandial rise in blood glucose and reduced body weight modestly . Given the ease of administration and high levels of tolerance, BTI320 has the potential to be used as an adjunct to lifestyle modification for diabetes prevention.