# ITCA 650 Significantly Reduces the Need to Advance Antidiabetes Therapy Compared to Sitagliptin

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#### **ABSTRACT**

**Background:** The need to advance antidiabetes therapy is a valid indicator of the effectiveness and sustainability of an antidiabetes agent. ITCA 650 is an osmotic mini-pump in development for type 2 diabetes (T2D) that continuously delivers exenatide SC for up to 6 months after subdermal placement. ITCA 650 20 mcg/day for 13 weeks followed by a maintenance dose of 60 mcg/day every 6 months was tested vs sitagliptin 100 mg (SITA) in the FREEDOM-2 study. ITCA 650 demonstrated greater reductions in HbA1c (1.5 % vs 0.8%, *P*<0.001) and body weight (4 kg vs 1.3 kg, *P*<0.001).

**Methods:** This exploratory analysis from FREEDOM-2 assessed the need for further therapy in addition to ITCA 650 or SITA added to metformin in 530 uncontrolled T2D pts (mean baseline HbA1c 8.6%). Further therapy was protocol mandated based on predefined criteria that became more stringent over time including any HbA1c >8% after Week 26.

**Results:** More SITA pts advanced therapy compared to ITCA 650; the incidence increased significantly and progressively with SITA after Week 26. In contrast, most ITCA 650 treated pts achieved and maintained glycemic control. At 52 weeks, 85.2% of pts on ITCA 650 remained on two therapies (Met + ITCA 650) compared to 64.6% on SITA.

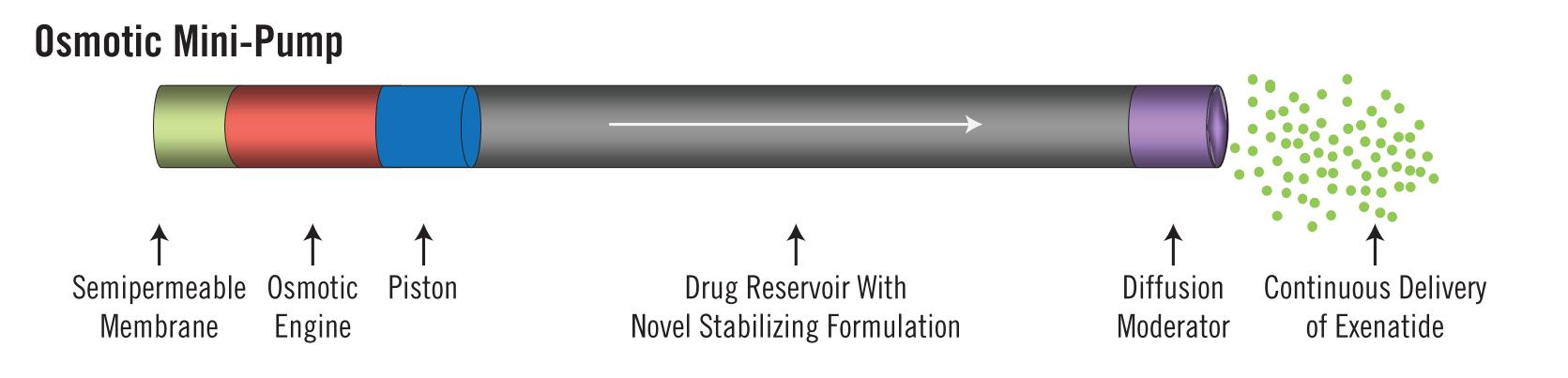
**Summary:** In conclusion, addition of ITCA 650 for 52 weeks led to better sustained glycemic control in uncontrolled T2D on metformin, significantly reducing the need for further therapy compared to addition of SITA.

## INTRODUCTION

- Patients with type 2 diabetes frequently require advancement of therapy beyond initial metformin treatment to achieve treatment goals.
- Although numerous drugs are available for the individualized management of type 2 diabetes, poor treatment adherence, sub-optimal efficacy, inadequate weight control, and unacceptable tolerability remain barriers to optimal glycemic control.<sup>1-3</sup>
- Despite its wide use, sitagliptin glucose-lowering effects are relatively modest, but most notably, persistent treatment effects are not achieved with sitagliptin as add-on to metformin as reported in clinical trials<sup>4</sup> and observed in real-world setting.<sup>5</sup>
- GLP-1 receptor agonists are effective therapeutic agents for the treatment of T2D; the need to administer by injection may limit their use early in treatment.
- Adherence to treatment with antidiabetic drugs is generally low, and is reported to range from 38% to 54% with GLP-1 agonists.<sup>6</sup>
- In addition to the negative impact on achieving effective glycemic control, poor medication adherence results in increased healthcare costs. 1-2
- ITCA 650 is an investigational drug device combination product that consists of an osmotic mini-pump (**Figure 1**) that provides continuous subcutaneous (SC) delivery of exenatide for up to 6 months after its subdermal placement in the abdominal wall.
- Exenatide plasma levels are maintained as long as the ITCA 650 device is in situ, and no action is required on the part of patient.

- Placement and removal of ITCA 650 is performed by trained healthcare professionals in a brief office procedure. The sterile mini-pump is placed in the sub-dermis of the abdominal wall using a placement tool and is removed or replaced through a small (~5 mm) incision and closed with Steri-Strips.
- Phase 3 studies with ITCA 650 demonstrated significant improvement in change from baseline HbA1c, body weight, and HbA1c<7% compared with placebo or sitagliptin in patients with type 2 diabetes.<sup>7,8</sup>

#### Figure 1. ITCA 650 Osmotic Mini-Pump

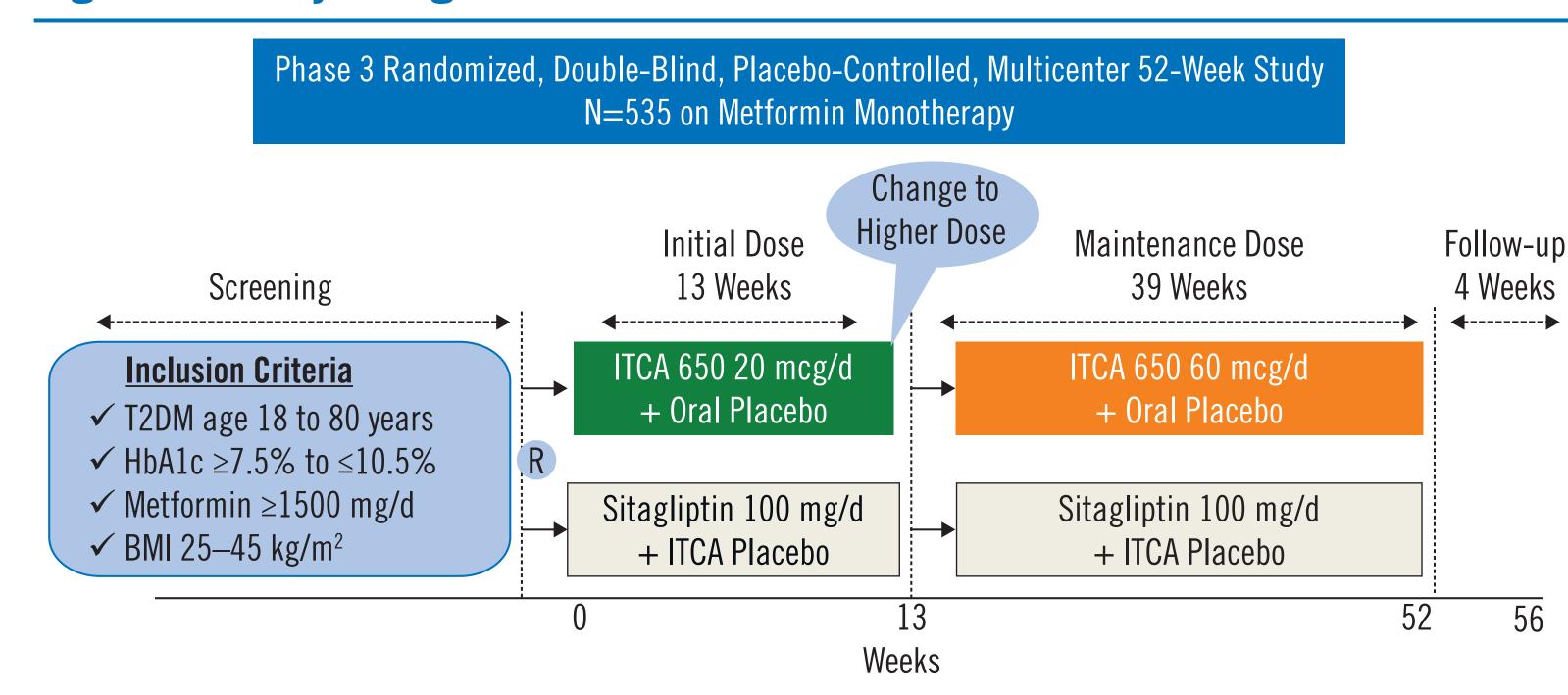


• ITCA 650 releases drug at a predetermined rate based on osmosis. Extracellular fluid enters through the semi-permeable membrane directly into the osmotic engine (salt gradient). The resulting pressure pushes the piston at a slow and consistent rate of travel that forces the drug formulation to be released through the orifice of the diffusion moderator.

### OBJECTIVE

- To assess the need to advance antidiabetes therapy, a meaningful measure of the effectiveness and sustainability of antidiabetes therapy, in patients with type 2 diabetes treated with ITCA 650 vs. sitagliptin.<sup>8</sup>
- Analysis of data from FREEDOM-2 a randomized, double-blind, double-dummy study comparing ITCA 650 and sitagliptin (**Figure 2**).

Figure 2. Study Design for FREEDOM-2



#### METHODS

• Descriptive statistics on disposition, demographic and baseline characteristics of patients who need to advance antidiabetes therapy compared to the overall patient population are provided below.

- Data from patients with type 2 diabetes, uncontrolled on metformin (n=263 on ITCA 650, n=257 on sitagliptin) were analyzed for the proportion of patients needing advancement of antidiabetes therapy.
- Rescue, requiring advancement of therapy, the addition of or increase of therapy from baseline, was protocol mandated based on predefined criteria.
- Day 0 to Week 13:
- Two or more fasting self-monitored blood glucose (SMBG) values >240 mg/dL during any
   7-day period
- Two consecutive FPG values >240 mg/dL
- After Week 13:
- Two or more fasting SMBG values >200 mg/dL during any 7-day period;
- Two consecutive FPG values >200 mg/dL
- An HbA1c elevation of  $\geq 1.5\%$  at any timepoint in the study
- An HbA1c >8.0% after Week 26
- Data were analyzed for the modified intent-to-treat population (mITT), which included all patients who initiated study treatment (had a procedure started for placement of ITCA 650/ITCA placebo or took sitagliptin/sitagliptin placebo) and who had a valid baseline and at least 1 post baseline HbA1c value.

# RESULTS

- FREEDOM-2 previously demonstrated significant improvement with ITCA 650 60 mcg/d vs. sitagliptin 100 mg/d in HbA1c, body weight, the composite endpoint of a reduction of >0.5% in HbA1c and weight loss ≥2 kg from baseline, and the proportion of patients achieving HbA1c <7%.</li>
- LS mean change (SE) from baseline for HbA1c at Week 52 was -1.5% (0.08) with ITCA 650 vs. -0.8% (0.08) with sitagliptin (*P*<0.001 for ITCA 650 vs. sitagliptin) from a baselne of 8.5% and 8.7%, respectively (**Figure 3**).

Figure 3. LS Mean (SE) Change From Baseline to Week 52 for HbA1c (%) – mITT Population

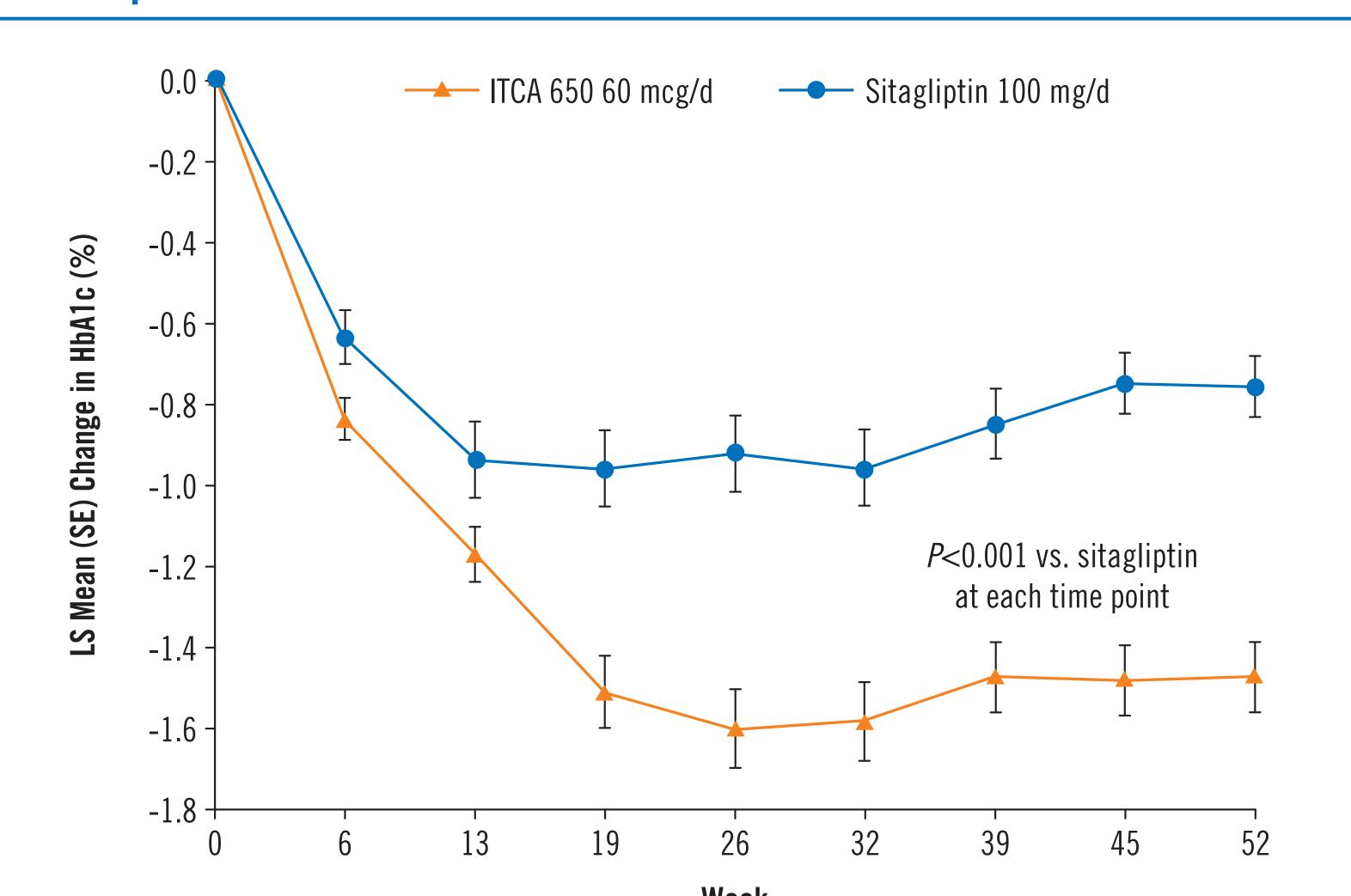


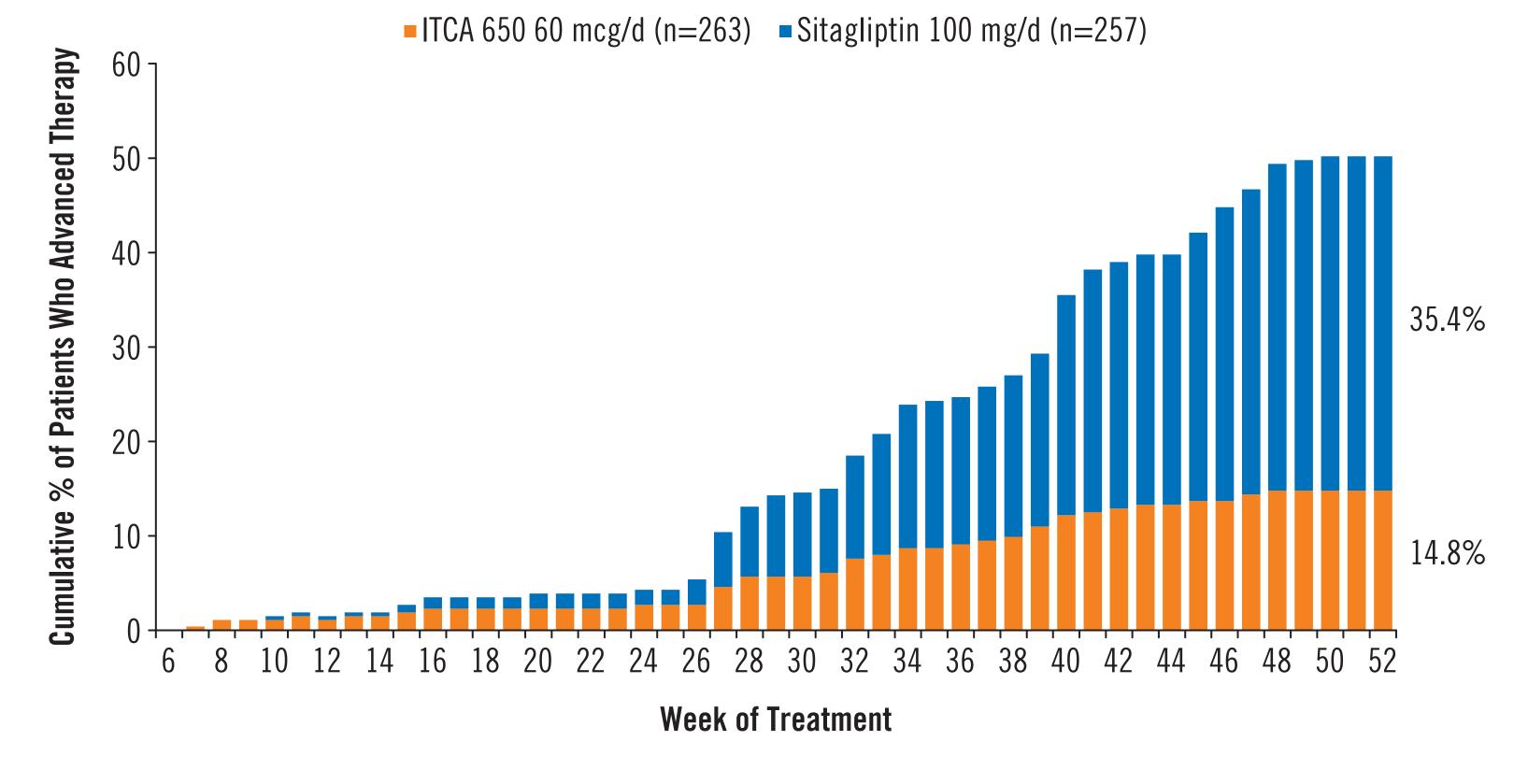
Table 1. Baseline Demographic and Clinical Characteristics for Population Requiring Advancement of Therapy vs. Overall Study – mITT Population

	Advanced Therapy Population		Overall Study (mITT Population)	
	ITCA 650 20/60 mcg/d	Sitagliptin 100 mg/d	ITCA 650 20/60 mcg/d	Sitagliptin 100 mg/d
Number	39	91	263	257
Age, years <sup>a</sup>	$53.6 \pm 9.6$	$54.7 \pm 10.0$	$55.4 \pm 9.8$	$54.6 \pm 10.3$
Male, (%)	53.9%	51.7%	54.4%	59.5%
Hispanic or Latino, (%)	48.7%	50.6%	42.6%	42.0%
Race, (%)				
White	82.1%	78.0%	76.0%	76.7%
Black/African American	10.3%	14.3%	11.4%	12.5%
Other	7.6%	7.7%	12.6%	10.8%
Body weight, kg <sup>a</sup>	$93.7 \pm 20.4$	$91.2 \pm 20.0$	$92.2 \pm 19.9$	$92.0 \pm 21.4$
BMI, kg/m <sup>2 a</sup>	$33.1 \pm 6.0$	$32.7 \pm 5.7$	$32.8 \pm 5.6$	$32.4 \pm 5.6$
HbA1c (%) <sup>a</sup>	$9.1 \pm 1.0$	$8.9 \pm 0.9$	$8.5 \pm 0.9$	$8.7 \pm 0.9$
Time since diabetes diagnosis (years) <sup>a</sup>	$9.0 \pm 5.5$	$8.2 \pm 5.4$	$8.8 \pm 6.1$	$7.8 \pm 5.4$
Metformin dose at baseline (mg/day) <sup>a</sup>	2009 (258)	2004 (287)	2033 (261)	2014 (284)

Table 2. HbA1c and Body Weight Prior to Advancement of Therapy

	Mean (standard error)		
	ITCA 650 60 mcg/d N=39	Sitagliptin 100 mg/d N=91	
HbA1c, %	$8.7 \pm 0.14$	$8.8 \pm 0.09$	
Mean change HbA1c, %	$-0.37 \pm 0.21$	-0.08 0.11	
Body weight, kg	$91.6 \pm 3.4$	$89.7 \pm 2.1$	
Mean change Body Weight, kg	$-2.1 \pm 0.6$	$-1.5 \pm 0.4$	

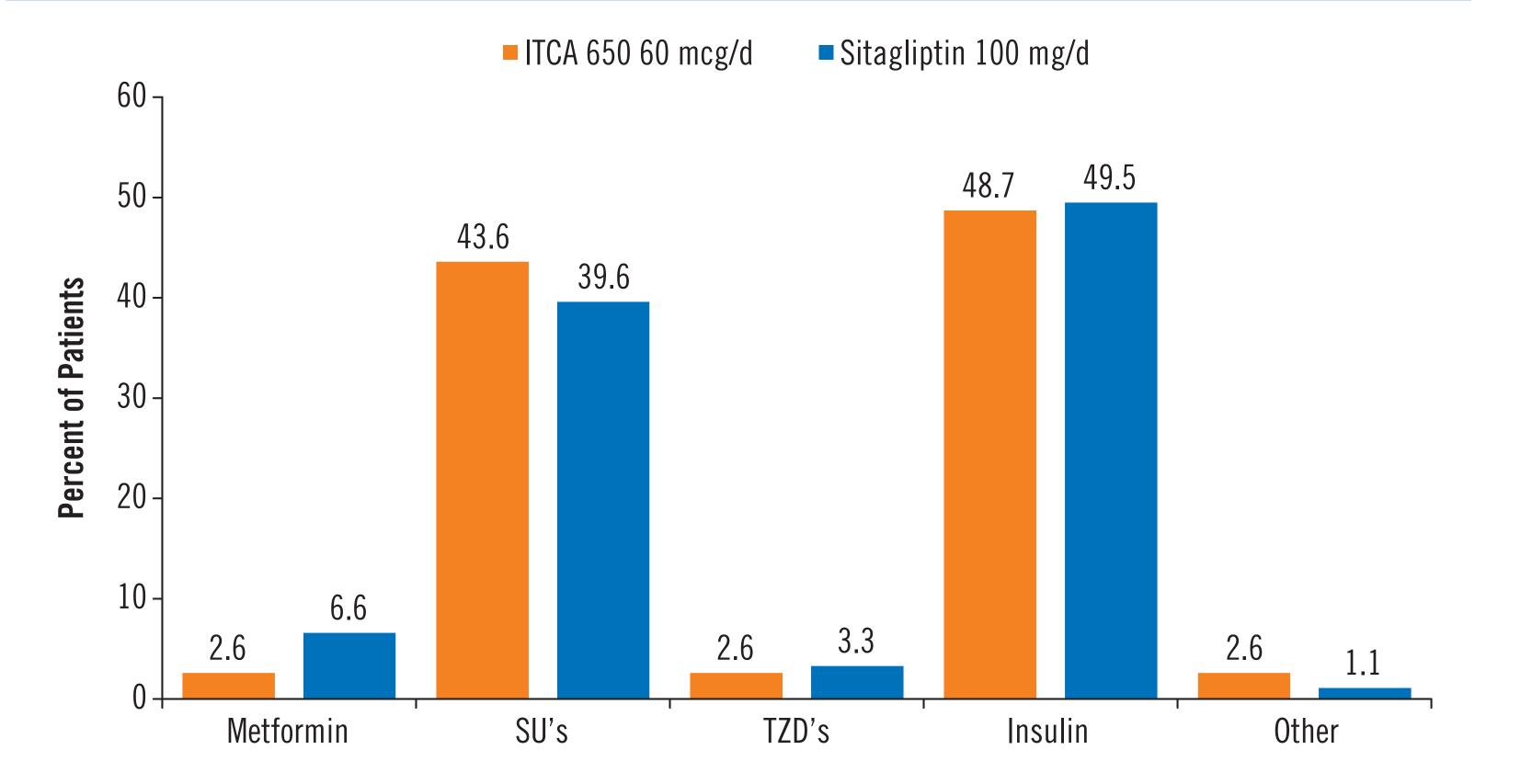
Figure 4. Percent of Patients Who Advanced Therapy by Week of Treatment (mITT Population)



- At baseline, demographic and clinical characteristics of patients who required AT were comparable to the overall study population (Table 1).
- At Week 52, 15% of the ITCA 650 group and 35% of the sitagliptin group required rescue necessitating advancement of therapy (**Figure 4**).
- An increase in the incidence of patients who advanced therapy was seen in both groups at Week 26 as the criteria became more stringent.
- Most (85%) ITCA 650 treated patients remained on assigned therapy at Week 52. (**Figure 4**).
- In contrast, a progressive increase in the need to advance therapy was observed in the sitagliptin group after Week 26 (**Figure 4**).

• Drugs most often used to advance therapy were insulin and sulfonylureas (mITT Population) (Figure 5).

Figure 5. Medications Used to Advance Therapy (mITT Population)



#### SUMMARY

- In this global study of patients who were poorly controlled on optimal doses of metformin, greater efficacy (HbA1c, weight, and goal attainment) was achieved with ITCA 650 compared to sitagliptin.
- Nearly 35% of patients on treatment with sitagliptin + metformin needed to advance therapy compared with 15% of patients treated with ITCA 650 + metformin.
   The need to advance therapy with sitagliptin was incremental and progressive over time.
- The need to advance therapy with sitagliptin was incremental and progressive over time compared to ITCA 650.
- By Week 52, nearly 85% of better controlled patients in the ITCA 650 group remained on metformin alone compared to nearly 65% of patients in the sitagliptin group.
- This is consistent with sustained efficacy over time of ITCA 650 compared to sitagliptin.

#### CUNCLUSIUN

• In this prespecified analysis of a randomized, controlled study in inadequately controlled type 2 diabetes patients on maximal or near maximal doses of metformin, add-on therapy with ITCA 650 resulted in significantly improved and sustained glycemic control without the need to further advance therapy in most patients.

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