SAKURA 1 and 2 Phase 3 Pivotal Studies

DaxibotulinumtoxinA for Injection (RT002) for the Treatment of Moderate to Severe Glabellar Lines

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Authors and Disclosures

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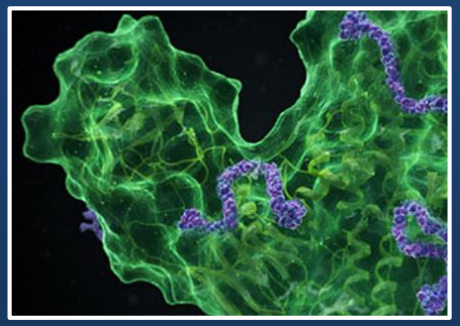
Revance's Differentiated Neuromodulator

One
THERAPEUTIC AGENT

DaxibotulinumtoxinA



Highly purified, botulinum toxin type A molecule

+

Unique
EXCIPIENT

Patented Stabilizing Peptide

Positively charged peptide that binds with negatively charged area of molecule.
NO animal-derived components or human albumin

Two
'DAXI' MODALITIES

Current Focus

DaxibotulinumtoxinA for Injection (RT002)

- In late-stage development
- Designed to be long lasting, injectable neuromodulator

DaxibotulinumtoxinA Topical Gel (RT001)

- In preclinical development
- Designed to offer topical delivery of botulinum toxin

Potential for Better, Longer, Safer Treatment

DaxibotulinumtoxinA for Injection (RT002) is an investigational product
DaxibotulinumtoxinA Topical Gel (RT001) is an investigational product

BELMONT[1] Glabellar Lines Results Positive DaxibotulinumtoxinA Demonstrates Long-Lasting Duration of Effect

Duration Highlights

6-month median duration of ≥ 1-point improvement as measured by IGA-FWS in the daxibotulinumtoxinA 40U dose, with 23.6 weeks vs.18.8 weeks for onabotulinumtoxinA (p=0.030)

At 24 Weeks:

- DaxibotulinumtoxinA 40U and 60U doses continued to deliver clinically meaningful higher response rates vs. onabotulinumtoxinA as assessed by IGA-FWS and GAIS
  - More specifically, daxibotulinumtoxinA 40U results indicate 31% of subjects maintain None or Mild wrinkle severity on IGA-FWS vs. onabotulinumtoxinA at 12%

Safety: DaxibotulinumtoxinA 40U appeared generally safe and well-tolerated with no ptosis

Next Steps: BELMONT results support selection of daxibotulinumtoxinA 40U dose to move forward into Phase 3 (SAKURA)

[1]Carruthers, J., *et al*. Injectable DaxibotulinumtoxinA for the Treatment of Glabellar Lines: A Phase 2, Randomized, Dose-Ranging, Double-Blind, Multicenter Comparison with OnabotulinumtoxinA and Placebo. *Dermatol. Surg*. 2017; 43: 1321 – 1331

DaxibotulinumtoxinA for Injection (RT002) is an investigational product

SAKURA 1 and 2 Study Objectives and Endpoints

Two Pivotal Phase 3 Studies Identical in Design

Study Objective: To evaluate the efficacy and safety of a single treatment of DaxibotulinumtoxinA for Injection (Daxi) 40U for the treatment of moderate to severe glabellar lines compared to placebo

Primary Endpoint*: Proportion of subjects achieving a score of 0 or 1 (None or Mild) and an improvement of ≥ 2 points from baseline on both the IGA-FWS** and PFWS† scales concurrently at Week 4 (2-Point Composite Response)

Key Secondary Endpoints*

- Proportion of subjects who achieve a score of 0 or 1 (None or Mild) on IGA-FWS and PFWS through Week 24
- Median duration: time to loss of none or mild wrinkle severity on both IGA-FWS and PFWS
- Median duration: time to return to baseline wrinkle severity on both IGA-FWS and PFWS

Exploratory Efficacy Endpoint*

- Median duration: ≥1-point improvement from baseline on IGA-FWS

*SAP designated Intent to Treat (ITT) analysis as primary; **Investigator Global Assessment-Facial Wrinkle Severity;
†Patient Facial Wrinkle Severity

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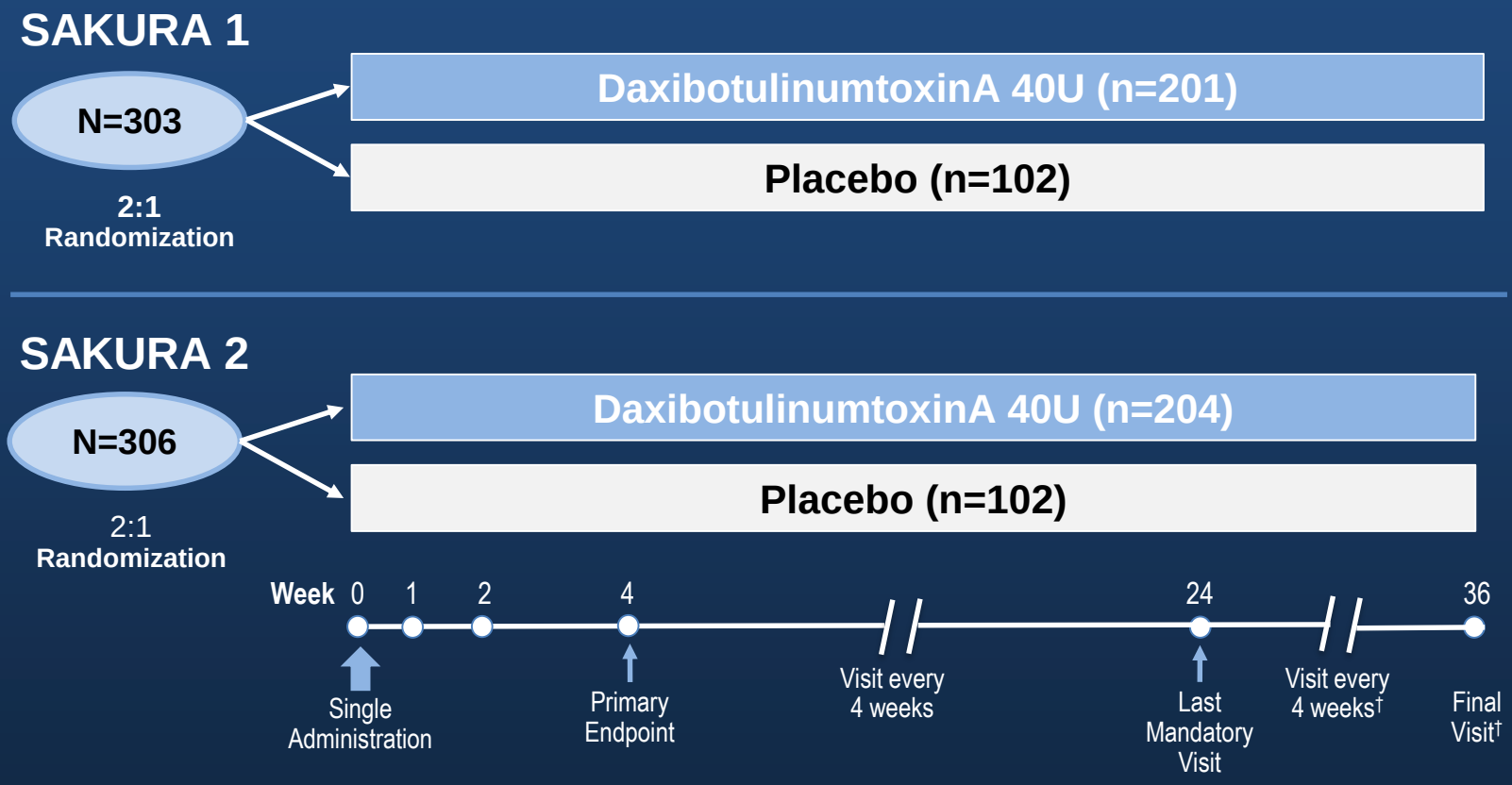
SAKURA 1 and 2 Study Designs

Evaluating Subjects over 36 weeks across 30 Sites in US and Canada



†Until both IGA-FWS and PFWS return to baseline

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SAKURA 1 and 2 Frown Wrinkle Severity Scales

Both investigators and subjects trained at trial initiation on a validated 4-Point Wrinkle Severity Scale to assess severity of glabellar frown lines

At entry, subjects were required to have glabellar line wrinkle severity of either **Moderate or Severe** as assessed by both the investigator and subject

Investigator Global Assessment-Frown Wrinkle Severity (IGA-FWS) Scale

IGA-FWS	
Rating Score	**Frown Wrinkle Severity**
0	None
1	Mild
2	**Moderate**
3	**Severe**

Patient Frown Wrinkle Severity (PFWS) Scale

PFWS		
Rating Score	**Frown Wrinkle Severity**	**Description**
0	None	No wrinkles
1	Mild	Very shallow wrinkles
2	**Moderate**	**Moderate wrinkles**
3	**Severe**	**Deep wrinkles**

SAKURA 1 and 2 Subject Disposition and Analysis Populations

Two Pivotal Phase 3 Studies Identical in Design

	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=102)	Daxi 40U (n=204)
Subject Disposition				
Completed Week 4	97 (95.1%)	196 (97.5%)	99 (97.1%)	203 (99.5%)
Completed Week 24	91 (89.2%)	188 (93.5%)	93 (91.2%)	199 (97.5%)
Completed the Study	93 (91.2%)	182 (90.5%)	93 (91.2%)	191 (93.6%)
Analysis Population				
Intent-to-treat (ITT)	102 (100%)	201 (100%)	102 (100%)	204 (100%)
Safety	102 (100%)	201 (100%)	101 (99.0%)*	205 (100.5%)*

*A placebo subject who received Daxi in error was included in the Daxi group for safety summary.

SAKURA 1 and 2 Demographics

Treatment Population Similar to Other Phase 3 Trials with Botulinumtoxin Type A in Glabellar Lines

	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=102)	Daxi 40U (n=204)
Female, n (%)	88 (86.3%)	174 (86.6%)	87 (85.3%)	183 (89.7%)
Hispanic/Latino Ethnicity	25 (24.5%)	47 (23.4%)	10 (9.8%)	19 (9.3%)
Race				
White	81 (79.4%)	173 (86.1%)	92 (90.2%)	180 (88.2%)
Black/African American	8 (7.8%)	10 (5.0%)	3 (2.9%)	9 (4.4%)
Asian	2 (2.0%)	7 (3.5%)	5 (4.9%)	11 (5.4%)
Other	11 (10.8%)	11 (5.5%)	2 (2.0%)	4 (2.0%)

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SAKURA 1 and 2 Demographics

Treatment Population Similar to Other Phase 3 Trials with Botulinumtoxin Type A in Glabellar Lines

	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=102)	Daxi 40U (n=204)
Age (years), mean (SD) range	49.0 (11.13) 22--74	50.9 (11.22) 23--74	50.5 (9.98) 27--75	49.6 (9.84) 21--73
18—45 years	32 (31.4%)	58 (28.9%)	30 (29.4%)	62 (30.4%)
>45—55 years	41 (40.2%)	68 (33.8%)	42 (41.2%)	91 (44.6%)
>55—75 years	29 (28.4%)	75 (37.3%)	30 (29.4%)	51 (25.0%)

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SAKURA 1 and 2 Baseline Characteristics

Treatment Groups Were Well-Balanced within Each Study and Included Both Treatment-Naïve and Treatment-Experienced Subjects

	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=102)	Daxi 40U (n=204)
Prior BoNT-A*, n (%)	45 (44.1%)	92 (45.8%)	60 (58.8%)	121 (59.3%)
Months since last BoNT-A* mean (SD) range	22.6 (19.61) 1--94	32.2 (37.05) 7--205	23.0 (24.36) 7--121	22.7 (23.67) 7--193
IGA-FWS at Maximum Frown				
Moderate	66 (64.7%)	123 (61.2%)	67 (65.7%)	129 (63.2%)
Severe	36 (35.3%)	78 (38.8%)	35 (34.3%)	75 (36.8%)
PFWS at Maximum Frown				
Moderate	64 (62.7%)	120 (59.7%)	49 (48.0%)	106 (52.0%)
Severe	38 (37.3%)	81 (40.3%)	53 (52.0%)	98 (48.0%)

*Botulinum toxin type A

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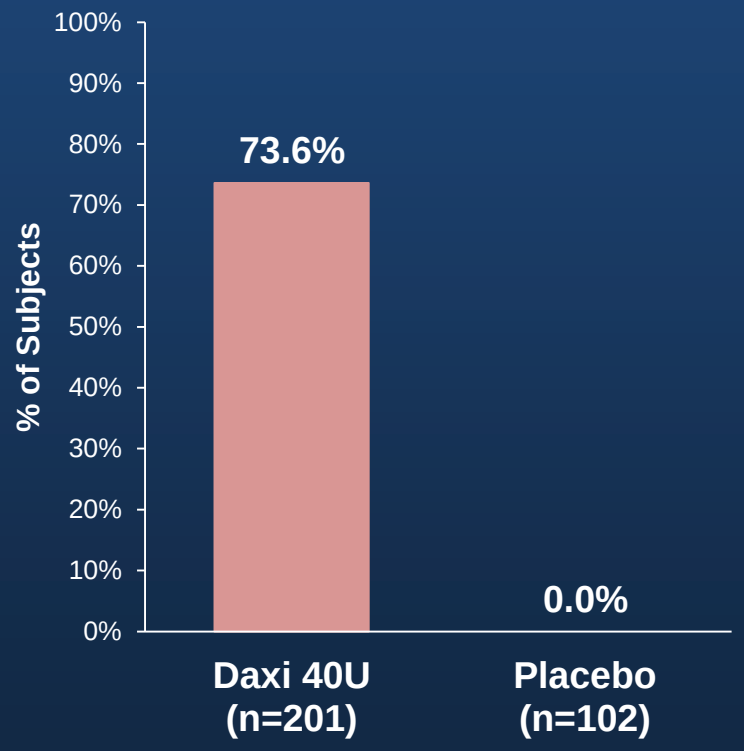
SAKURA 1 and 2 Primary Endpoint at Week 4

Proportion of Subjects Who Achieve > 2-Point Composite Response at Max Frown

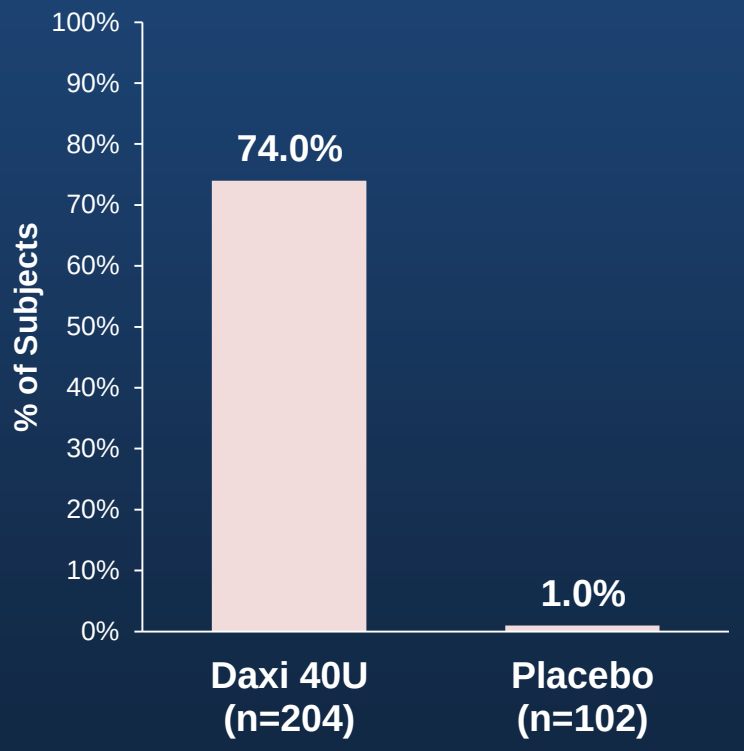
Two-Point Composite Response of 74% Achieved in Both Pivotal Phase 3 Studies

SAKURA 1



**p < 0.0001 (vs Placebo)*

SAKURA 2



**p < 0.0001 (vs Placebo)*

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SAKURA 1 and 2 Secondary Endpoint

None or Mild Response Rate on IGA-FWS and PFWS over Time

Robust Response Rates Observed on Key None or Mild Outcome Measure at All Time Points through Week 24 in Both Pivotal Studies

Investigator Assessment (IGA-FWS)

Week	SAKURA 1		SAKURA 2	
	Daxi 40U (n=201)	Placebo (n=102)	Daxi 40U (n=204)	Placebo (n=102)
2	93.5%*	3.9%	98.0%*	2.0%
4	97.5%*	4.9%	97.5%*	3.9%
8	91.5%*	7.8%	94.6%*	2.9%
12	84.1%*	2.9%	88.2%*	2.9%
16	71.1%*	5.9%	74.0%*	2.9%
20	53.2%*	2.9%	54.4%*	2.9%
24	35.3%*	2.0%	29.4%*	2.0%

p < 0.0001 (vs Placebo)

Patient Assessment (PFWS)

Week	SAKURA 1		SAKURA 2	
	Daxi 40U (n=201)	Placebo (n=102)	Daxi 40U (n=204)	Placebo (n=102)
2	92.5%*	3.9%	91.2%*	3.9%
4	92.0%*	1.0%	90.2%*	3.9%
8	84.6%*	2.0%	85.3%*	6.9%
12	72.6%*	2.9%	71.6%*	5.9%
16	57.2%*	5.9%	53.4%*	5.9%
20	44.8%*	2.9%	35.8%*	6.9%
24	23.9%*	1.0%	21.6%*	2.0%

p < 0.0001 (vs Placebo)

Note: Cochran-Mantel-Haenszel test stratified by study center was used for response rate comparison for Daxi vs Placebo at each time point on ITT population. Missing data were imputed with worst post-baseline outcome for Daxi and best outcome for Placebo.

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SAKURA 1 and 2 and BELMONT[1] Phase 2 Study Results

None or Mild Response on IGA-FWS over Time

Investigator Assessment (IGA-FWS)

Week	SAKURA 1 Daxi 40U (n=201)	SAKURA 2 Daxi 40U (n=204)	BELMONT[1] Daxi 40U (n=39)	BELMONT[1] Onabot[2] 20U (n=42)
2	93.5%*	98.0%*	97.3%**	95.2%**
4	97.5%*	97.5%*	97.4%**	92.9%**
8	91.5%*	94.6%*	97.4%**	83.3%**
12	84.1%*	88.2%*	84.6%**	69.0%**
16	71.1%*	74.0%*	66.7%**	31.7%**
20	53.2%*	54.4%*	46.2%**	22.0%**
24	35.3%*	29.4%*	30.8%**	11.9%*

*$p < 0.0001$ (vs Placebo)

**$p < 0.01$ (vs Placebo)

[1]Carruthers, J., *et al*. Injectable DaxibotulinumtoxinA for the Treatment of Glabellar Lines: A Phase 2, Randomized, Dose-Ranging, Double-Blind, Multicenter Comparison with OnabotulinumtoxinA and Placebo. *Dermatol. Surg*. 2017; 43: 1321 – 1331. [2]OnabotulinumtoxinA.

Note: Presentation of trial data for reference only. Cochran-Mantel-Haenszel test stratified by study center was used for response rate comparison for Daxi vs Placebo at each time point on ITT population. Missing data were imputed with worst post-baseline outcome for Daxi and best outcome for Placebo.

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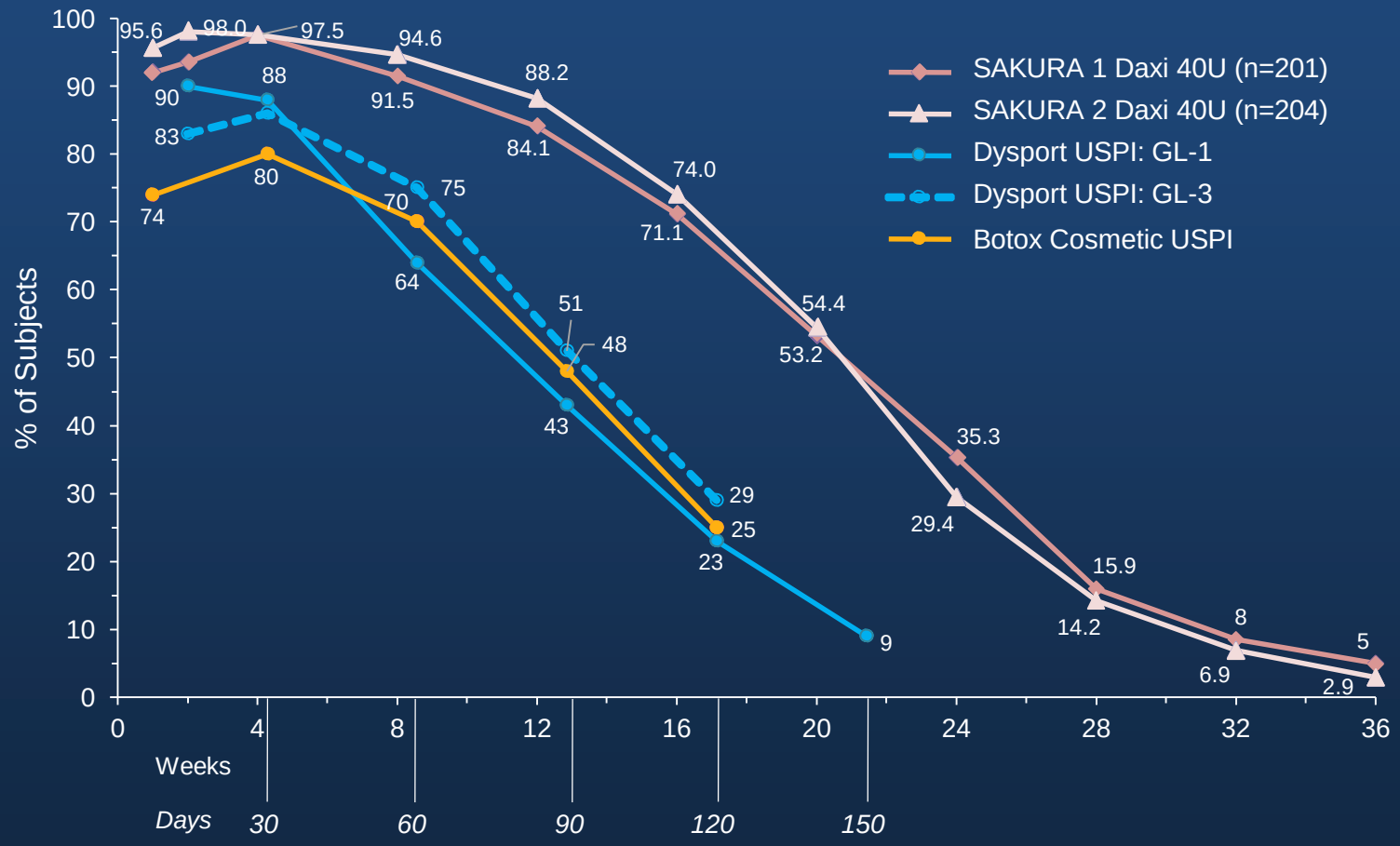
SAKURA 1 and 2 Results and Botox® Cosmetic and Dysport ® USPI[1] Data

None or Mild Response Rates on 4-Point Investigator Assessment over Time



[1]United States Prescribing InformationPhase 3 Studies in GL for each neuromodulator with data available through at least Day 120 conducted separately and presented for reference only. USPI: US Package Insert. Note: In SAKURA (ITT), missing data were imputed with the worst post-baseline outcome (or best outcome for Placebo arm) on visits up to Week 24. Non-responder imputation was used for visits post Week 24.

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None or Mild Response Definition
Descriptor of Clinically Meaningful Effect

None or Mild (Score of 0 or 1) is described as one of the required elements used establish efficacy in the FDA's **"Guidance for Industry Upper Facial Lines: Developing Botulinum Toxin Drug Products" (August 2014)**

- Score of 0 or 1 *and*
- Two-grade improvement from the baseline, on both the Investigator and Subject scales concurrently, to ensure clinical significance

IGA-FWS	
Rating Score	**Frown Wrinkle Severity**
0	None
1	Mild
2	Moderate
3	Severe

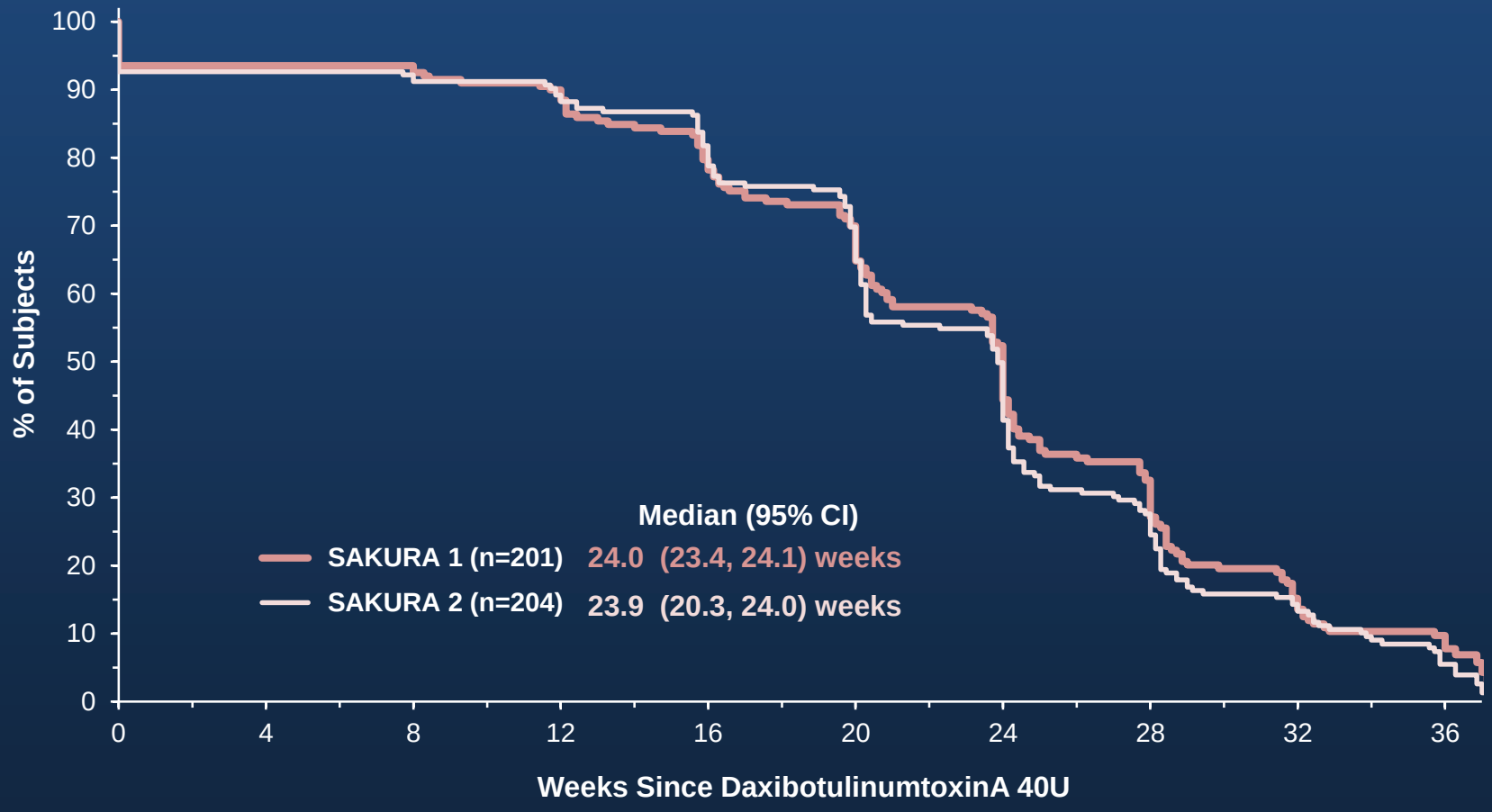
PFWS		
Rating Score	**Frown Wrinkle Severity**	**Description**
0	None	No wrinkles
1	Mild	Very shallow wrinkles
2	Moderate	Moderate wrinkles
3	Severe	Deep wrinkles

None or Mild response rate information has been used in Botox and Dysport USPIs as the basis for their duration language

SAKURA 1 and 2 Secondary Endpoint

Time to Loss of None or Mild Wrinkle Severity on Both IGA-FWS and PFWS

Median Duration of 24 Weeks Achieved for Time to Loss of None or Mild Wrinkle Severity in Both Pivotal Studies



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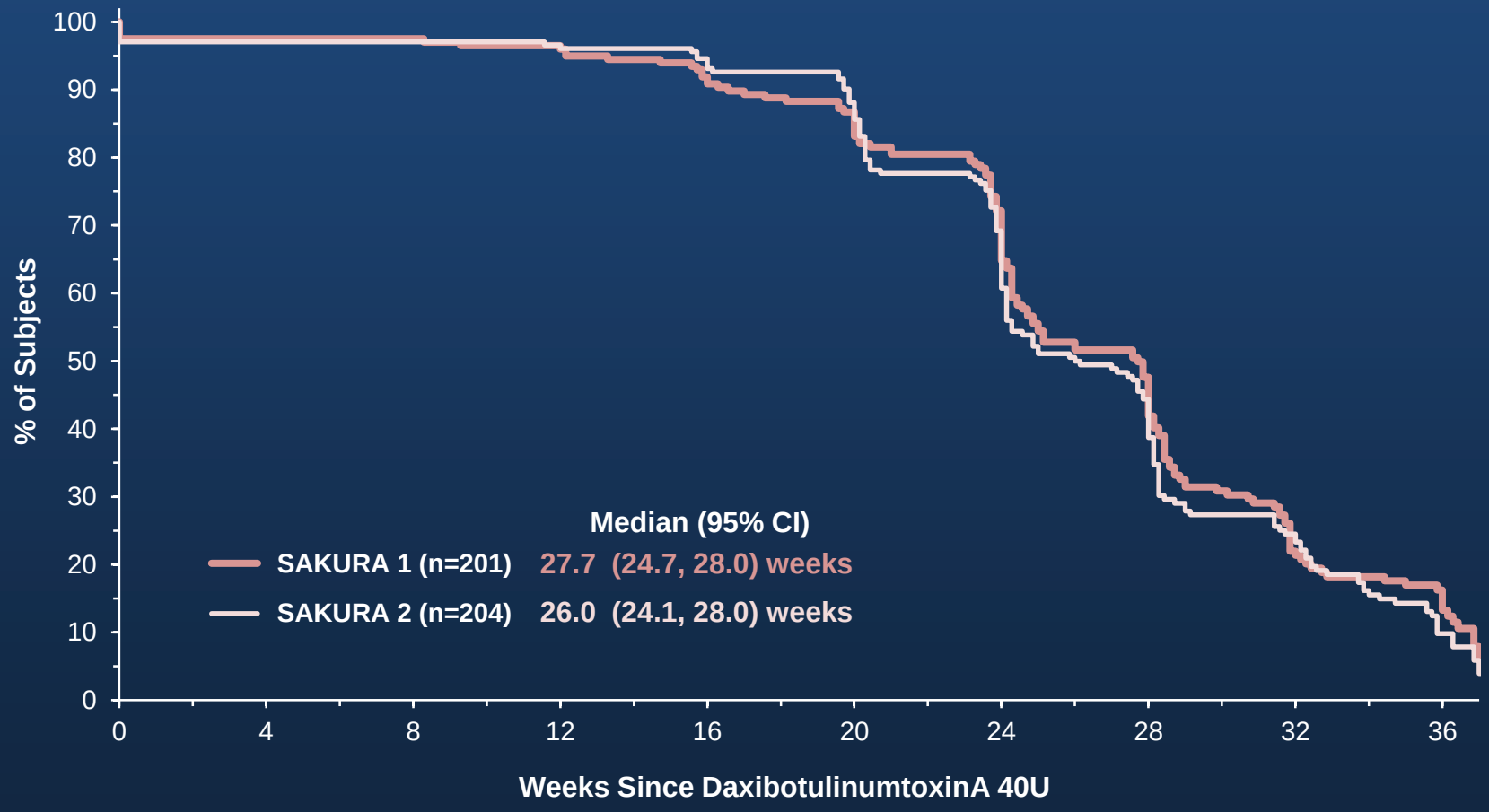
SAKURA 1 and 2 Secondary Endpoint
Time to Return to Baseline on Both IGA-FWS and PFWS

Median Duration of at Least 26 Weeks Observed for Time to Return to Baseline Wrinkle Severity in Both Pivotal Studies



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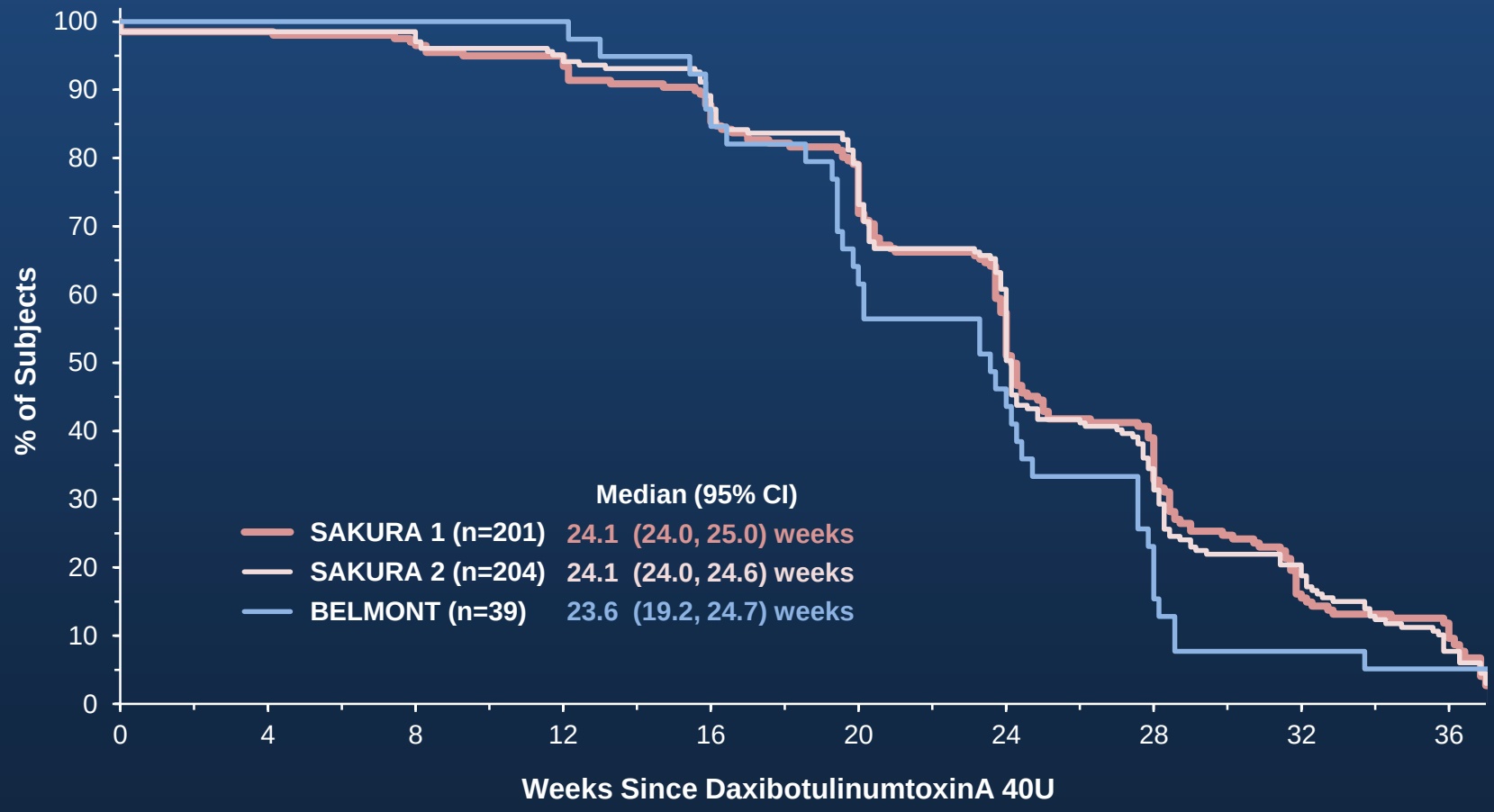
SAKURA 1 and 2 Exploratory Endpoint

Median Duration of ≥ 1 Point Improvement from Baseline on IGA-FWS

Median Duration of 24.1 Weeks Achieved for ≥ 1-Point Improvement in SAKURA 1 and 2 Confirmed Duration of Effect Observed in Phase 2 BELMONT Study



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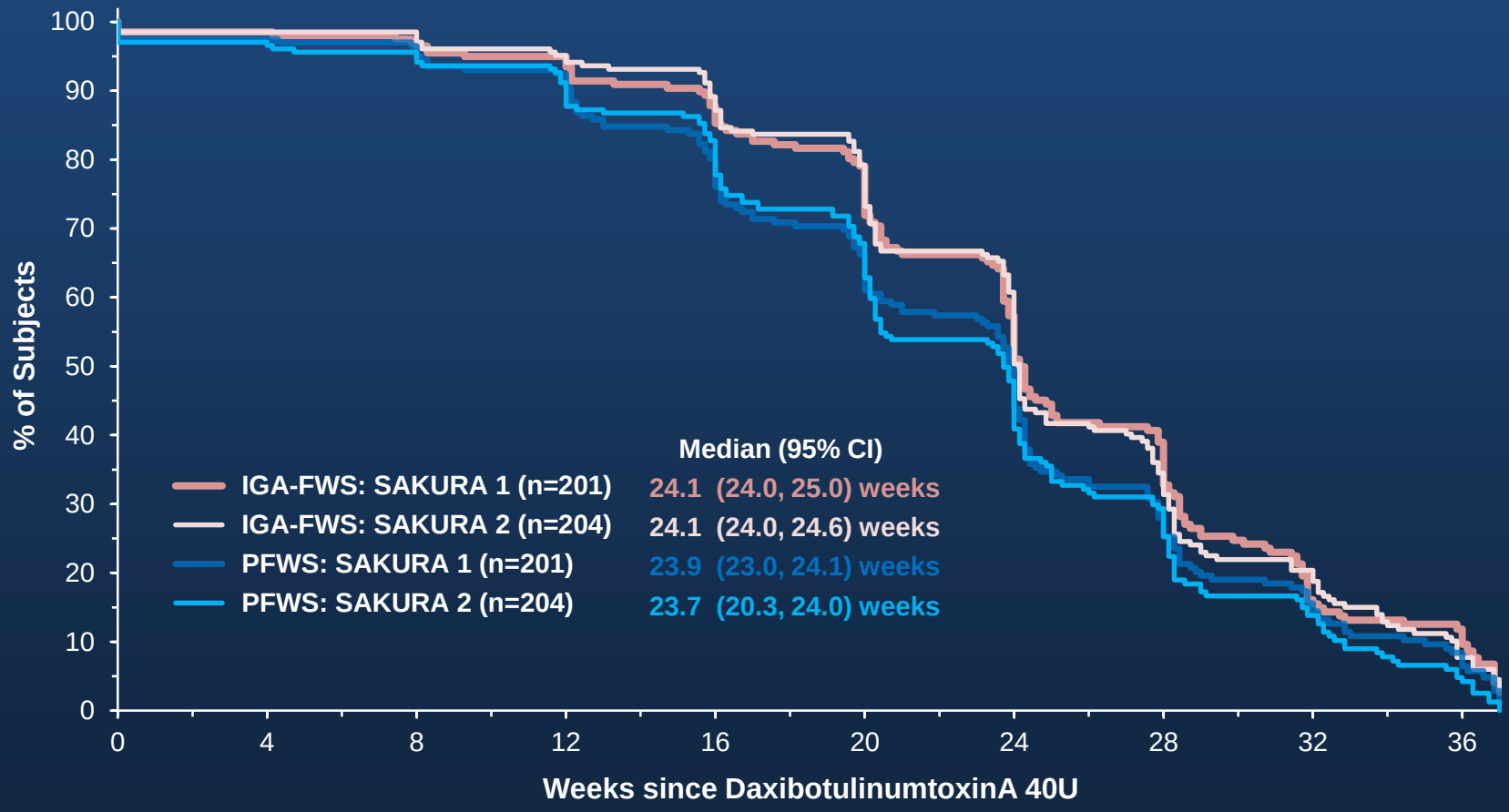
SAKURA 1 and 2 Exploratory Endpoint

Median Duration of ≥ 1 Point Improvement from Baseline on IGA-FWS and PFWS

Median Duration of 24 Weeks Achieved for ≥ 1-Point Improvement on IGA-FWS Confirmed on PFWS in Both Pivotal Studies



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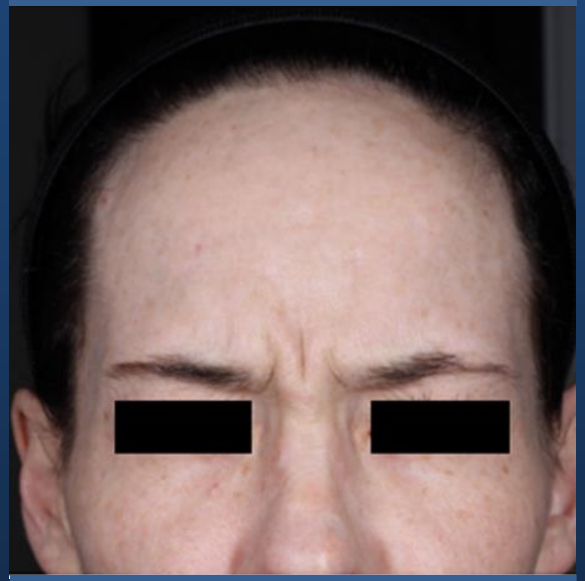
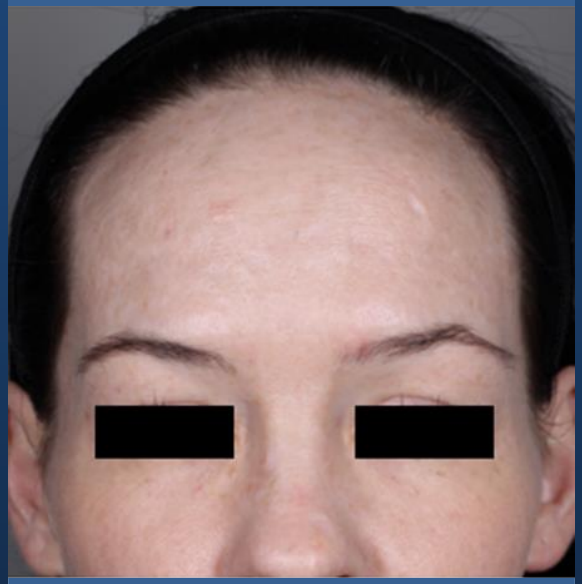
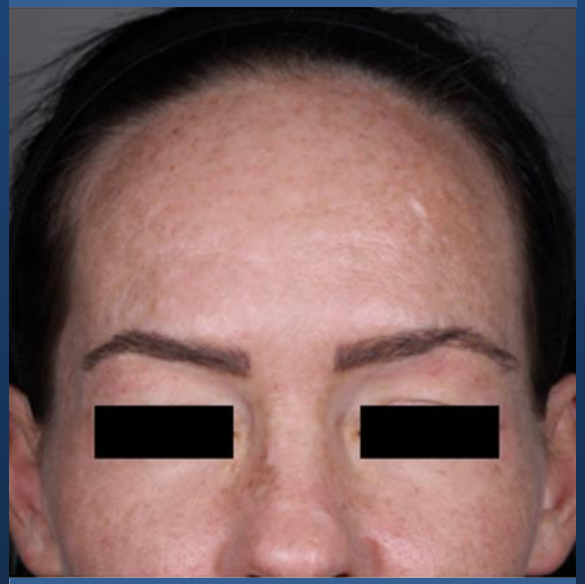
Example 3-Point Improvement by IGA-FWS & PFWS at Week 4

Three-Point Sustained Duration of Effect by IGA-FWS over 24 Weeks

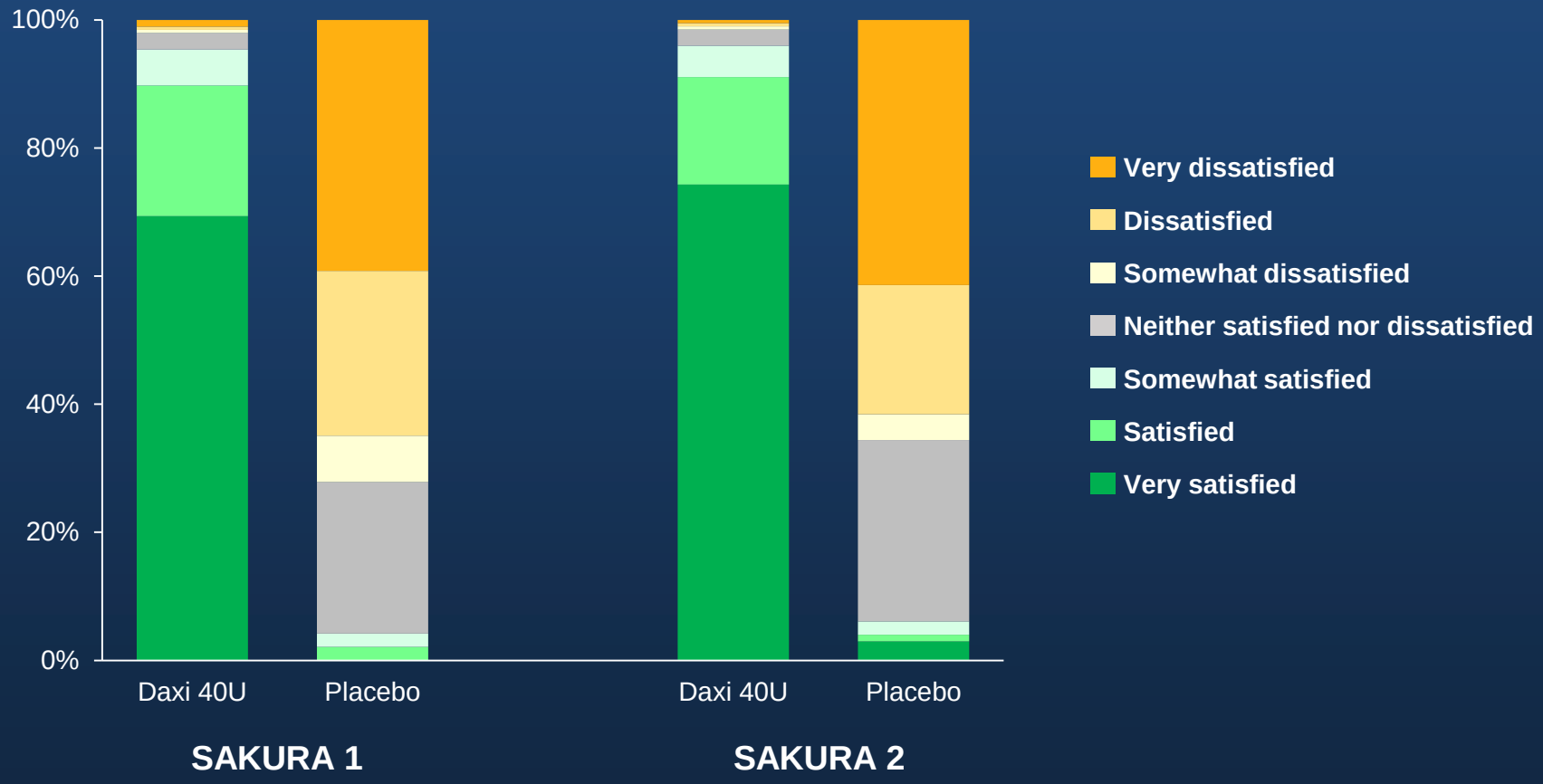
DaxibotulinumtoxinA 40U
MAXIMUM FROWN

Pre-treatment	Week 4	Week 24
		
Baseline Scores: IGA-FWS: 3 PFWS: 3	Week 4 Scores: IGA-FWS: 0 PFWS: 0	Week 24 Scores: IGA-FWS: 0 PFWS: 1
	Three Point Improvement from Baseline on Investigator and Subject Assessment	Three Point Improvement from Baseline on Investigator Assessment and Two Point Improvement on Subject Assessment

DaxibotulinumtoxinA for Injection (RT002) is an investigational product

SAKURA 1 and 2 Patient Global Satisfaction with Treatment at Week 4

Subject Ratings of 'Very Satisfied' or 'Satisfied' were 88% in SAKURA 1 and 91% in SAKURA 2



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SAKURA 1 and 2

Number of Treatment-Related AEs by Preferred Term (≥ 2 % in Any Arm)

Preferred Term	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=101)	Daxi 40U (n=205)**
Headache	3 (2.9%)	14 (7.0%)	1 (1.0%)	12 (5.9%)
Eyelid ptosis*	0	5 (2.5%)	0	4 (2.0%)
Injection site pain	4 (3.9%)	10 (5.0%)	4 (4.0%)	5 (2.4%)
Injection site erythema	0	0	4 (4.0%)	5 (2.4%)
Injection site oedema	0	1 (0.5%)	3 (3.0%)	5 (2.4%)

*6 cases of mild severity, 3 cases of moderate severity. All cases resolved without sequelae. Median duration of 58 days.
**A placebo patient who received Daxi in error was included in the Daxi group for safety summary.

SAKURA 1 and 2

Injection Site Evaluations: Immediate Reactions Post-Treatment

Treatment Visit, Post - Treatment	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=101)	Daxi 40U (n=205)†
Erythema	0	2 (1.0%)	4 (4.0%)	6 (2.9%)
Edema	1 (1.0%)	1 (0.5%)	3 (3.0%)	3 (1.5%)
Burning or Stinging (described by subject)	0	3 (1.5%)	2 (2.0%)	5 (2.4%)
Itching (described by subject)	0	2 (1.0%)	0	1 (0.5%)
Bruising	0	0	0	0

DaxibotulinumtoxinA for Injection (RT002) is an investigational product

SAKURA 1 and 2 Serious Adverse Events by Preferred Term*

Preferred Term	SAKURA 1		SAKURA 2	
	Placebo (n=102)	Daxi 40U (n=201)	Placebo (n=101)	Daxi 40U (n=205)†
Bone marrow failure	0	1 (0.5%)	0	0
Sepsis	0	1 (0.5%)	0	0
Anxiety	1 (1.0%)	0	0	0
Uterine perforation	0	0	0	1 (0.5%)
Leiomyosarcoma recurrent	0	0	1 (1.0%)	0
Uterine leiomyoma	0	0	0	1 (0.5%)

*None of the Serious AEs above were related to treatment
†A placebo patient who received Daxi in error was included in the Daxi group for safety summary

DaxibotulinumtoxinA for Injection (RT002) is an investigational product

SAKURA 1 and 2 Studies
Efficacy Summary

Both SAKURA 1 and 2 Phase 3 studies with DaxibotulinumtoxinA for Injection 40U met their primary endpoint and demonstrated duration of effect ≥ 24 weeks

Primary Endpoint met 2-point composite response at Week 4 of 74% with Daxi in both studies vs. 0% and 1% with placebo ($p<0.0001$) in SAKURA 1 and 2, respectively

High Patient Global Satisfaction Rates observed in both studies at Week 4

- Satisfaction rate of “Satisfied” or “Very Satisfied” of 88% and 91% observed for SAKURA 1 and 2, respectively, on 7-point scale

Key Secondary Endpoint: Robust response rates observed on None or Mild outcome measure at all Time Points through Week 24 in both Pivotal Studies

Investigator Assessment (IGA-FWS)

Week	SAKURA 1	SAKURA 2
	Daxi 40U	Daxi 40U
16	71.1%	74.0%
24	35.3%	29.4%

Patient Assessment (PFWS)

Week	SAKURA 1	SAKURA 2
	Daxi 40U	Daxi 40U
16	57.2%	53.4%
24	23.9%	21.6%

DaxibotulinumtoxinA for Injection (RT002) is an investigational product

SAKURA 1 and 2 Studies
Duration of Effect Summary

SAKURA 1 and SAKURA 2 are the first and only Phase 3 confirmatory studies in patients with moderate to severe glabellar lines that demonstrated median duration of ≥ 24 weeks on multiple clinically meaningful outcome measures

Time to loss of None or Mild wrinkle severity (Score of 0 or 1) with Daxi 40U on both IGA-FWS and PFWS replicated duration observed with ≥ 1 point improvement results

- Median duration of 24.0 weeks and 23.9 weeks in SAKURA 1 and 2, respectively

Time to return to baseline wrinkle severity with Daxi on both IGA-FWS and PFWS exceeds six months

- Median duration of 27.7 weeks and 26.0 weeks in SAKURA 1 and 2, respectively

Median duration of ≥ 1 point improvement from baseline of 24 weeks observed on IGA-FWS confirmed on patient PFWS assessment measure

- IGA-FWS: 24.1 weeks in both SAKURA 1 and SAKURA 2
- PFWS: 23.9 weeks in SAKURA 1 and 23.7 weeks in SAKURA 2
- BELMONT ≥ 1 point improvement on IGA-FWS: 23.6 weeks with Daxi 40U vs. 18.8 weeks with OnabotulinumtoxinA 20U ($p<0.03$)1

[1]Carruthers, J., *et al*. Injectable DaxibotulinumtoxinA for the Treatment of Glabellar Lines: A Phase 2, Randomized, Dose- Ranging, Double-Blind, Multicenter Comparison with OnabotulinumtoxinA and Placebo. *Dermatol. Surg*. 2017; 43: 1321 – 1331.

DaxibotulinumtoxinA for Injection (RT002) is an investigational product

SAKURA 1 and 2 Studies
Safety Summary

DaxibotulinumtoxinA 40U was observed to be generally safe and well-tolerated through week 36 in both pivotal studies

Percentage of subjects in SAKURA 1 and 2 with adverse advents in the Daxi group were 36% and 46%, respectively, and 25% and 24% in the placebo group, respectively

- Majority of events in the Daxi group were mild in severity and considered to be unrelated to study drug
- No subjects in the Daxi group discontinued secondary to AEs
- Two subjects in the Daxi group in each study experienced a serious AE, none of which were treatment related

Treatment-related AEs in SAKURA 1 and 2 occurred in 17% and 21% of subjects in the Daxi group, respectively, and 8% and 10% in the placebo group, respectively. In the Daxi group across both studies:

- Most common events were headache (5.9% - 7.0%) and injection site pain (2.4% - 5.0%)
- Rates of injection-related edema and erythema were < 2.4% and all cases were mild in severity
- Eyelid ptosis rate of 2.2% observed