DIABETIC RETINOPATHY MANAGEMENT 2020

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Disclosures

Dr. Gordon is a principal investigator on clinical trials sponsored by Regeneron Pharmaceuticals, Inc., Genentech, NIH, Apellis, Allergan, Novartis, Alcon, Amgen, Hemera, Stealth Biotherapeutics, IONIS, Santen, Aerpio, Zeiss

Dr. Gordon is a paid consultant of Santen pharmaceuticals and a member of the Data and Safety Monitoring Board (DSMB) of AVANTE study

There is no financial disclosure related to this presentation

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Causes of Vision Loss in Diabetic retinopathy

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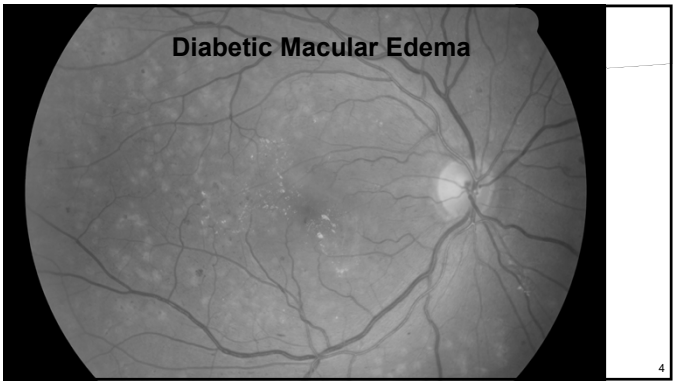

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Diabetic Macular Edema

Seen in both NPDR and PDR patients

Treatment

1. Anti VEGF
2. Laser – Thermal and Subtheshold
3. Steroids
4. Surgery in Tractional diabetic macular edema

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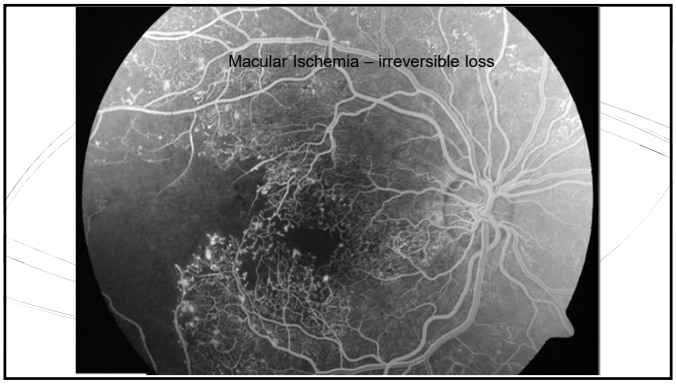

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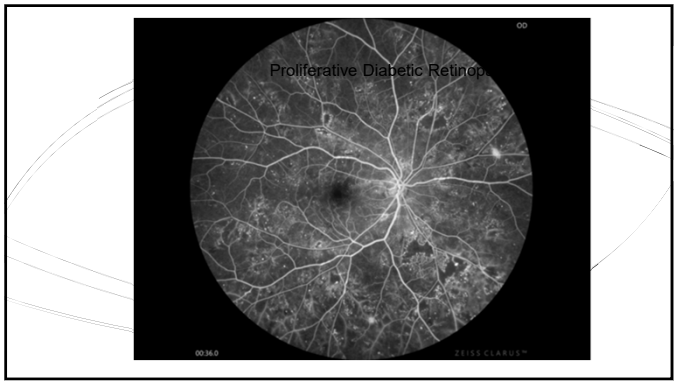

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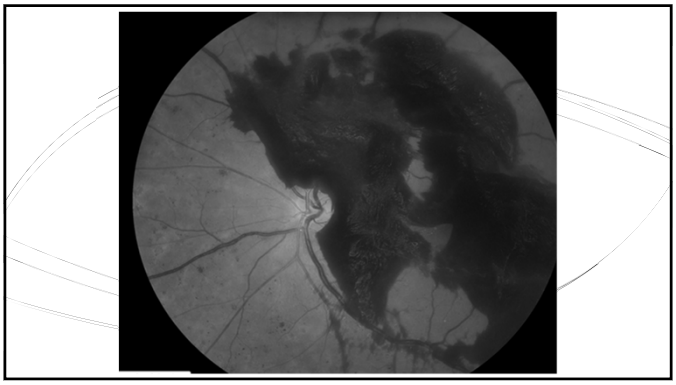

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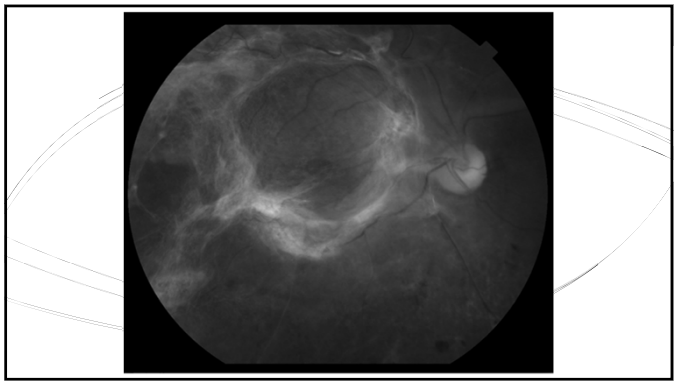

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Treatment for Proliferative Diabetic Retinopathy

1. Panretinal photocoagulation and/or

2. Anti VEGF

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Treatment is actively recommended for patients with Vision threatening conditions such:

- Center –involved macular edema
- Proliferative diabetic retinopathy

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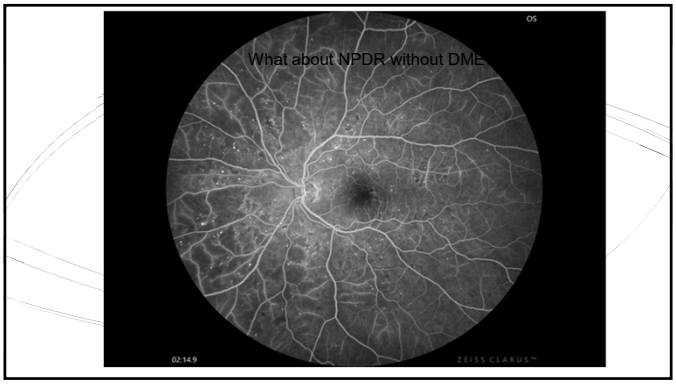

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International Clinical Diabetic Retinopathy Disease Severity Scale Detailed Table

LEVEL	SEVERITY
10	DR absent
20	Microaneurysms only
35	Mild NPDR
43	Moderate NPDR
47	Moderately severe NPDR
53	Severe NPDR
61	Mild PDR
65	Moderate PDR
71	High Risk PDR
75	High Risk PDR
81	Advanced PDR, fundus partially obscured, center of macula attached
85	Advanced PDR, posterior fundus obscured or center of macula detached
90	Cannot grade, even sufficiently for level 81 or 85

DRSS grading scale was derived from the ETDRS and is used to grade severity of DR and describe the change in severity over time.

ETDRS Group, #12 1991

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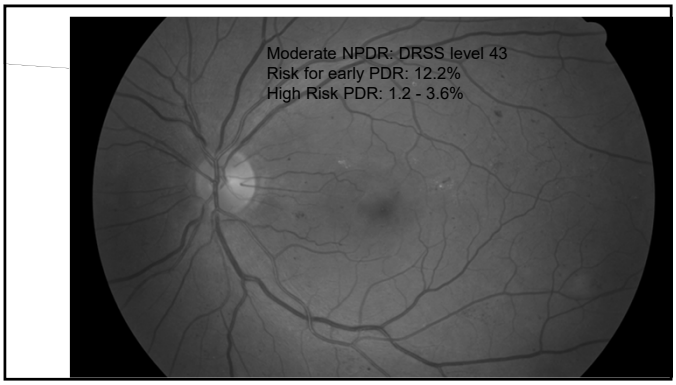

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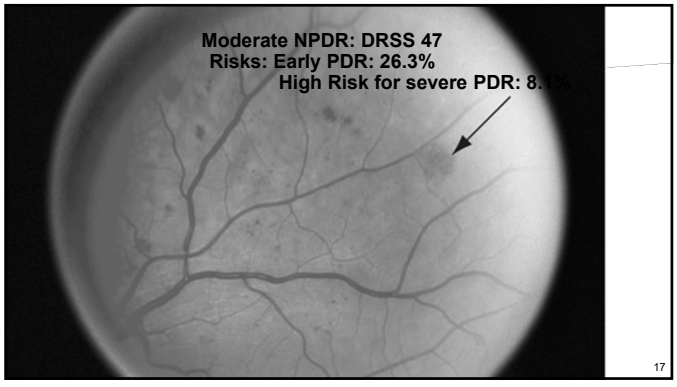

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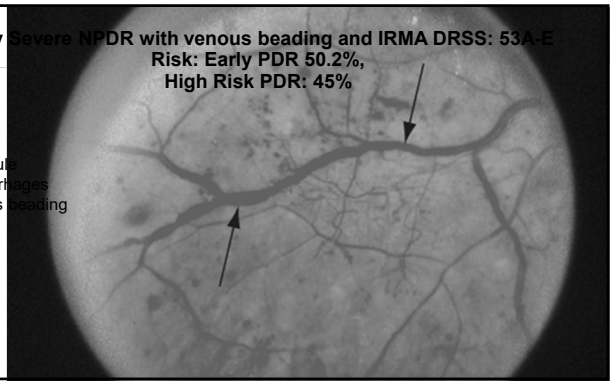
Very Severe NPDR with venous beading and IRMA DRSS: 53A-E
Risk: Early PDR 50.2%,
High Risk PDR: 45%



4:2:1 rule
Hemorrhages
Venous beading
IRMA's

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Diabetes Control and Complications Trial

- Randomized, multicenter study
- Compares the effect of intensive versus conventional blood sugar control in the progression of diabetic retinopathy
- Enrolled patients with or without NPDR

Intensive blood sugar control reduced the progression to severe NPDR or PDR in 47% *

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Barriers to achieving intensive blood sugar control

1. Insurance
2. Cost
3. Non compliance
4. Side effects of intensive control

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Approved Treatment for NPDR without DME

Panretinal photocoagulation

Ranibizumab (RIDE/RISE study)

Aflibercept

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Vision-Threatening Proliferative Diabetic Retinopathy (PDR) Events in non-PDR (NPDR) with Diabetic Macular Edema (DME)

Presented by **Carmelina Gordon, MD**
on behalf of the **VISTA and VIVID study investigators**

Specialty Eye Institute, Jackson, MI, USA

Presented at the American Academy of Ophthalmology Meeting, San Francisco, USA; October 12–15, 2019

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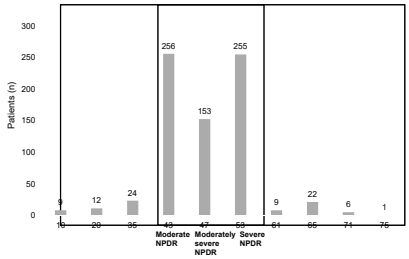
Analysis Groups



Incidence of PDR events was evaluated in patients with baseline DRSS scores of 10 to 53 (those without PDR at baseline)

Achievement of DRSS score of 35 or better was evaluated in patients with baseline DRSS scores of ≥43

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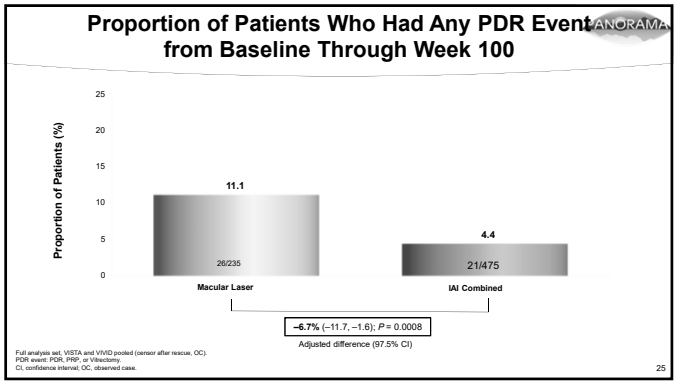

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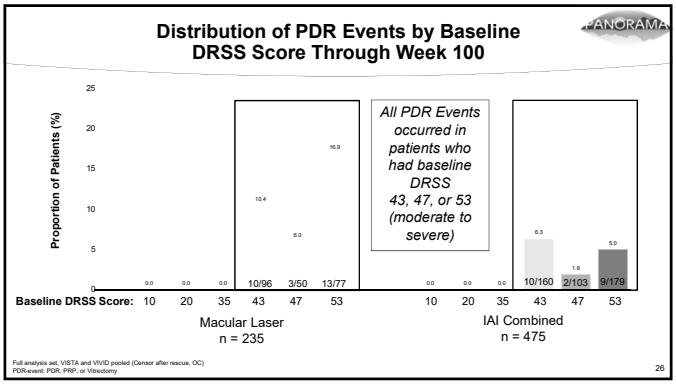

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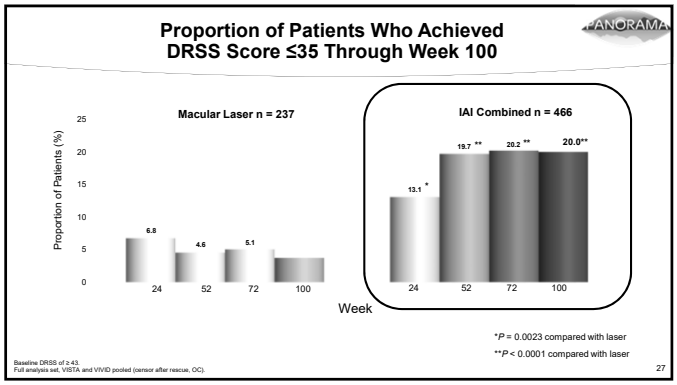

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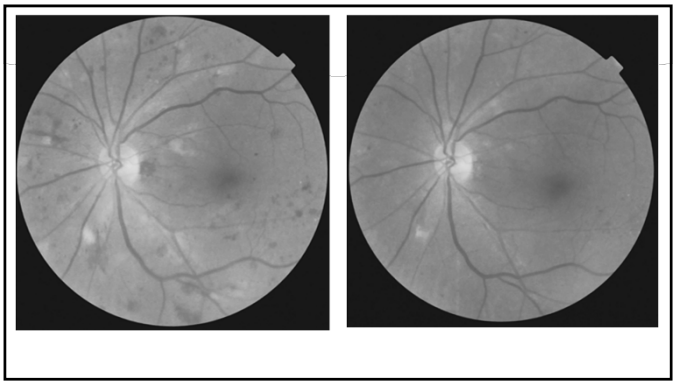

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Conclusions

IAI reduced the incidence of vision-threatening PDR events and increased the proportion of patients who achieved a DRSS score ≤35

- Significantly fewer patients treated with IAI had a PDR event compared with those treated with laser control
  - PDR events occurred significantly earlier in the macular laser group compared to the IAI group
- In both IAI and macular laser groups, all PDR events occurred in patients who had a baseline DRSS score of 43 or higher (moderate to severe NPDR)
- Significantly more patients treated with IAI achieved a DRSS score of 35 (mild NPDR) or better through week 100

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PANORAMA Study Design

Phase 3, double-masked, randomized study of efficacy & safety of IAI in patients with moderately severe to severe NPDR (DRSS level 47 and 53)
N = 402*

Sham
N = 133

2q16
IAI 2 mg every 16 weeks**
N = 135

2q8
IAI 2 mg every 8 weeks***
N = 134

Week 24
Primary endpoint: Proportion of patients improving ≥2 steps on DRSS
All IAI combined versus sham

Week 52
Primary endpoint: Proportion of patients improving ≥2 steps on DRSS
2q16 and 2q8 individually versus sham

Follow-up through Week 100

Key secondary endpoints
- % developing PDR/ASNV
- % developing CI-DME
- Time to development of PDR/ASNV or CI-DME

*Patients were stratified by baseline DRSS level; **After 3 initial monthly doses and 1 q8 interval; ***After 5 initial monthly doses, flexible treatment schedule after week 52.
2q8, 2 mg every 8 weeks; 2q16, 2 mg every 16 weeks; q8, every 8 weeks; ASNV, anterior segment neovascularization; CI-DME, center-involved diabetic macular edema; DRSS, Diabetic Retinopathy Severity Score; IAI, intravitreal aflibercept injection; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

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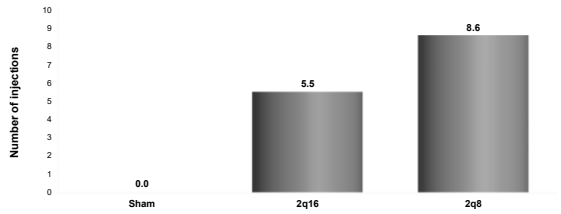
Treatment Experience through Week 52



Last observation carried forward (LOCF); sham n = 133, 2q16 n = 135, 2q8 n = 134.

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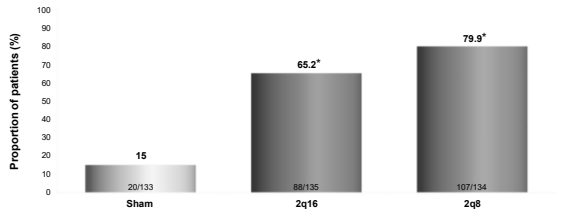
Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS at Week 52



LOCF; sham n = 133, 2q16 n = 135, 2q8 n = 134.

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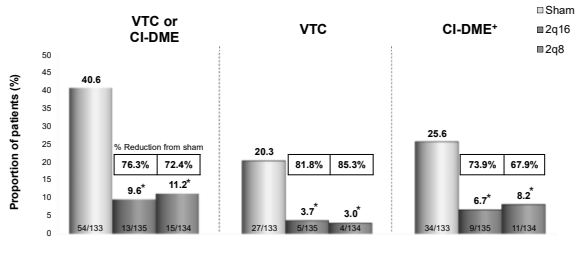
Proportion of Patients Developing a Vision-Threatening Complication or Center-Involved DME through Week 52



VTC = vision-threatening complication defined as PDR/ASNV; FAS; sham n = 133, 2q16 n = 135, 2q8 n = 134.

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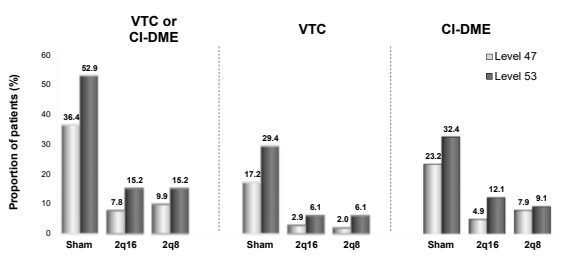
Proportion of Patients Developing a VTC or CI-DME through Week 52 by Baseline DRSS



VTC = vision-threatening complication defined as PDR/ASNV; FAS; sham n = 133, 2q16 n = 135, 2q8 n = 134.

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Patient Characteristics Affecting Incidence of VTC and CI-DME Events in Moderately Severe to Severe NPDR

A Post Hoc Analysis of PANORAMA

Carmelina Gordon MD, Richard Hamilton MD
on behalf of PANORAMA trial investigators

Accepted for presentation at the American Society of Retina Specialists meeting in Seattle, WA July 2020

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VTC (PDR/ASNV) Events

CI-DME Development

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Baseline characteristics studied

Demographics

Age
Ethnicity
BMI

Disease Characteristics

HgbA1c
Duration of Diabetes
DRSS level

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Summary of findings

VTC events
- Younger age
- Lower Hgb A1c
- Severe NPDR

CI- DME
- Older age
- Higher Hgb A1c
- Longer duration of DM
- Severe NPDR
- Hispanic ethnicity

No conclusion can be drawn from these associations due to small sample size

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Clinical data need to be tailored to "real world experience"

Obeid et al, (*Ophthalmology 2019 March ;126*)

76 eyes of 59 patients with PDR: 30 received anti VEGF; 46 received
Lost to follow up (more than 6 months)

Anti VEGF
Higher TRD 10
Iris Neovascularization 4

PRP
Less TRD 1
No *iris neovascularization*

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Clinical data need to be tailored to "real world experience"

Wubben et al, (Am J Ophthalmol 2019 Aug:204:13-18)
13 eyes of 12 patients received anti VEGF for the following Diagnoses:
7 PDR with DME;
3 PDR without DME;
3 moderate to severe NPDR with DME

Experienced treatment hiatus for 12 months
Reasons: intercurrent illness, non compliance, and lost of insurance

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Clinical data need to be tailored to "real world experience"

Complications upon follow up

Vitreous hemorrhage (9 eyes)

Neovascular glaucoma (5 eyes)

Tractional retinal detachment (4 eyes)

77% lost > 3 lines of vision with 46% having a final vision of hand motion or worse

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Summary

1. There is a rationale for treatment of non proliferative diabetic retinopathy without DME.
2. Certain baseline characteristics showed trends towards developing VTC (PDR/ASNV) and CI- DME.
3. Approved treatment modalities include intensive blood sugar control , panretinal photocoagulation and/or ranibizumab or aflibercept.
4. Treatment interruption with anti VEGF can result in devastating complications.

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