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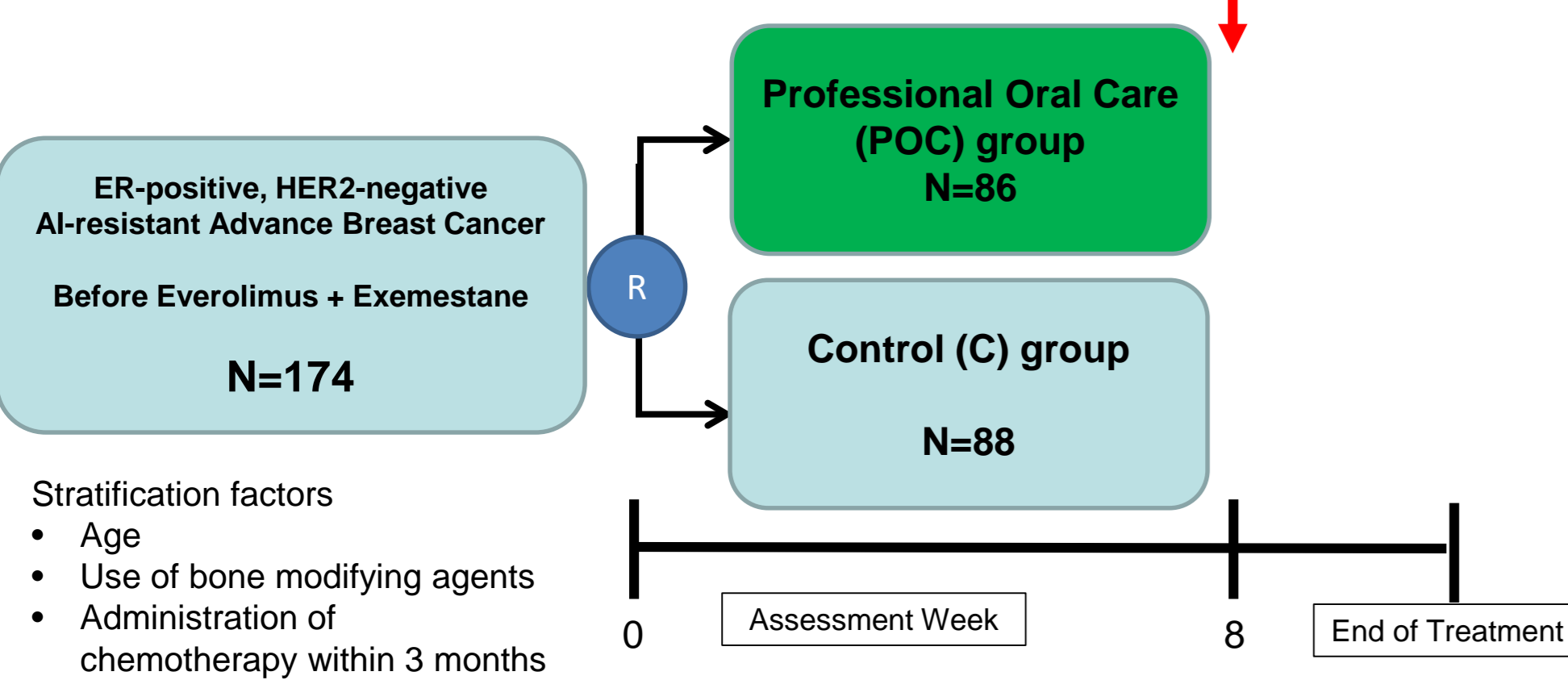
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Background

- Oral mucositis is a clinically significant complication of mucotoxic cancer therapy.
- The incidence of oral mucositis (any grade) as an adverse drug reaction of everolimus is 58%. In an analysis of Asian people, its occurrence was reported as 81%.
- Prophylactic professional oral health care reduces the risk of oral mucositis. This has been shown in a small prospective study that assessed the usefulness of prophylactic professional oral care for preventing mucositis in patients undergoing adjuvant chemotherapy.

Study Design

A multicenter, randomized, and controlled study. **Primary Endpoint**



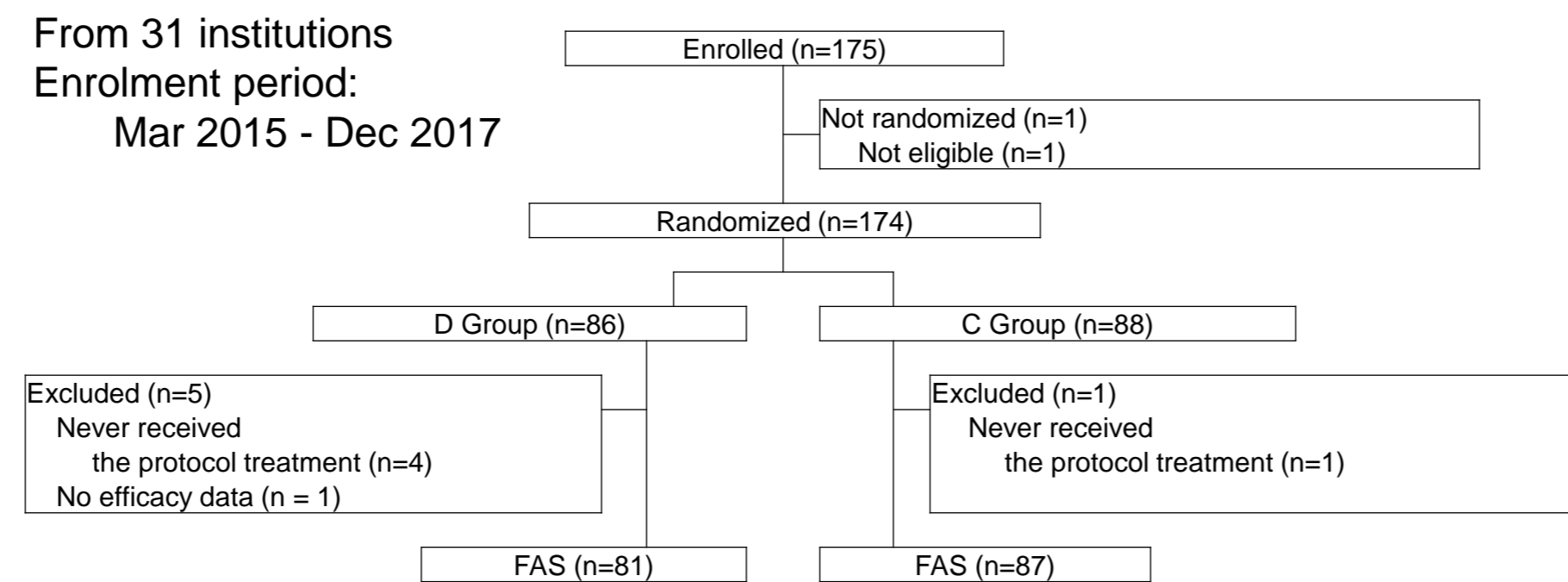
Procedure

POC group (Professional Oral Care)
: Scaling, crown polishing, brushing instruction, tongue plaque removal instruction, gargling instruction (0.2% Neostelin Green mouthwash solution), and dexaltin ointment use for grade 1 oral mucositis.

Control group (brushing instruction only group)
: Gargling instruction (physiological saline), brushing instruction, and use of oral mucositis ointment prohibited for grade 0, 1, and 2 oral mucositis.

- Interventions were provided by a licensed dentist or dental hygienist under the supervision of a dentist at 31 sites
- Training manuals were made to standardize the treatment of professional oral care.
- An oncologist and dentist evaluated each patient's oral mucositis every week for 8 weeks using CTCAE v3.0 for a comparison with BOLERO-2.

CONSORT Diagram



Patient Characteristics

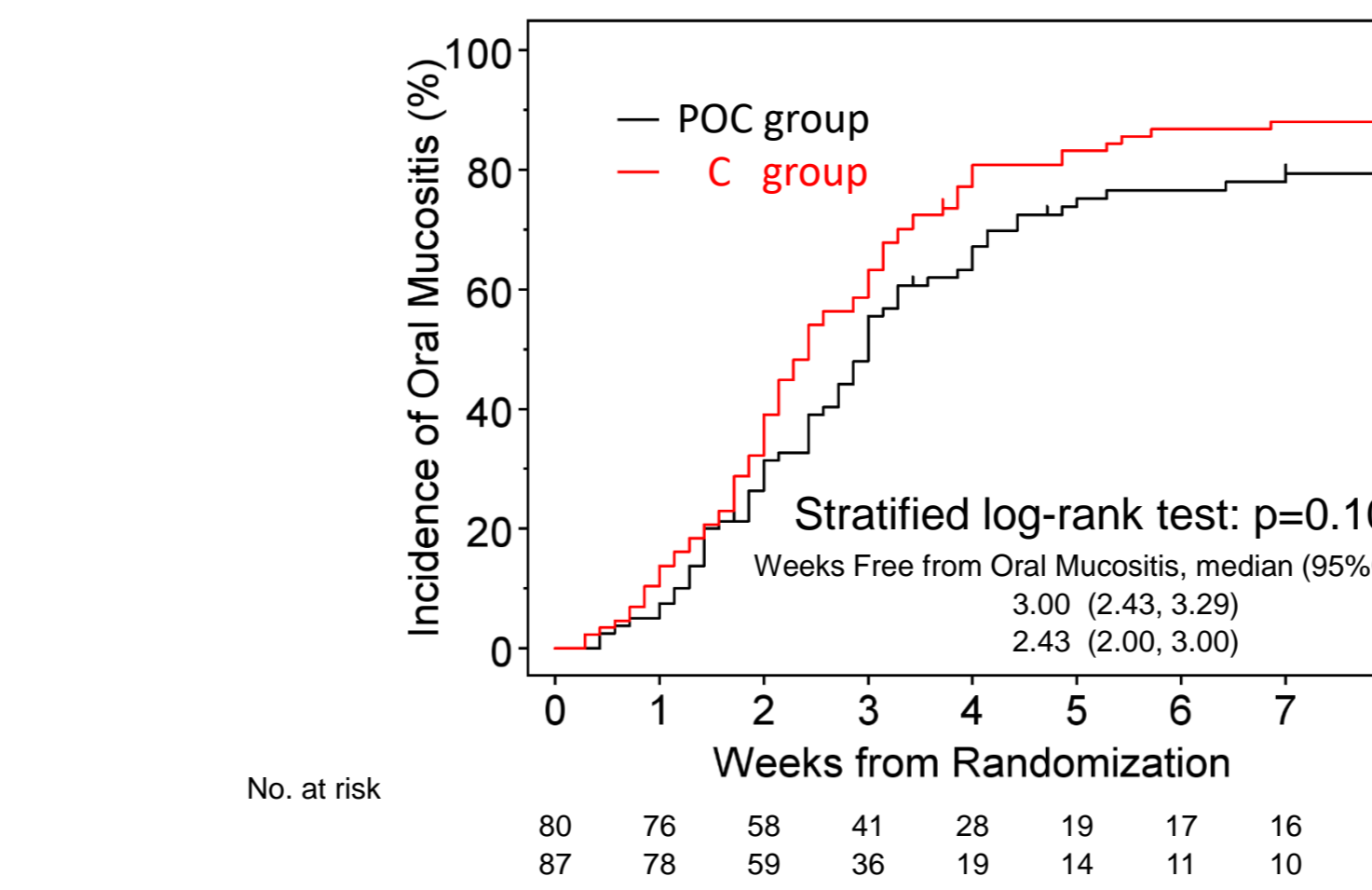
	POC Group (n=81)	C Group (n=87)	P-value
Age, n, mean (SD), median (min, max)	81, 63.6(7.5), 64.0(49, 84)	87, 62.9(8.9), 64.0(42, 83)	0.60 [†]
Age, n, %, (95% CI)			0.87 [†]
<65	42, 51.9(40.5, 63.1)	44, 50.6(39.6, 61.5)	
≥ 65	39, 48.1(36.9, 59.5)	43, 49.4(38.5, 60.4)	
Bone Modifying Agent, n, %, (95% CI)			0.78
Not used	39, 48.1(36.9, 59.5)	40, 46.0(35.2, 57)	
Used	42, 51.9(40.5, 63.1)	47, 54.0(43, 64.8)	
Chemotherapy for MBC, n, %, (95% CI)			0.57 [†]
Not used	73, 90.1(81.5, 95.6)	76, 87.4(78.5, 93.5)	
Used	8, 9.9(4.4, 18.5)	11, 12.6(6.5, 21.5)	
BMI (kg / m ²), n, %, (95% CI)			0.12 [†]
<25	54, 66.7(55.3, 76.8)	66, 75.9(65.5, 84.4)	
≥ 25	24, 29.6(20, 40.8)	21, 24.1(15.6, 34.5)	
Missing	3, 3.7(0.8, 10.4)	0, 0.0(0, 4.2)	
Smoking, n, %, (95% CI)			0.72 [†]
Non-smoker	75, 92.6(84.6, 97.2)	83, 95.4(88.6, 98.7)	
Smoker	4, 4.9(1.4, 12.2)	3, 3.4(0.7, 9.7)	
Missing	2, 2.5(0.3, 8.6)	1, 1.1(0, 6.2)	

Hypothesis and Study Objectives

- Hypothesis:**
The occurrence of oral mucositis will be reduced by the implementation of dental intervention prior to everolimus treatment in the form of tooth surface cleaning, scaling, oral hygiene instruction from a dental and oral surgeon, and the use of 0.2% Neostelin Green (Nippon Shika Yakuhin, Japan) mouthwash.
- Primary endpoint:** Incidence of oral mucositis (grade greater than or equal to 1)
 - Secondary endpoints:**
 - Incidence of oral mucositis (grade greater than or equal to 2) (evaluated by an oncologist and dentist);
 - incidence of oral mucositis (grade greater than or equal to 3) (evaluated by an oncologist and dentist);
 - incidence of oral mucositis (grade greater than or equal to 1) (evaluated by a dentist);
 - time to the onset of oral mucositis;
 - duration of each grade of oral mucositis;
 - each ratio of patients in suspension, or dose-reduction of everolimus treatment due to oral mucositis;
 - Oral Assessment Guide (Revised)¹;
 - Health-related quality of life (HRQOL);
 - and 9) time to treatment failure (TTF).

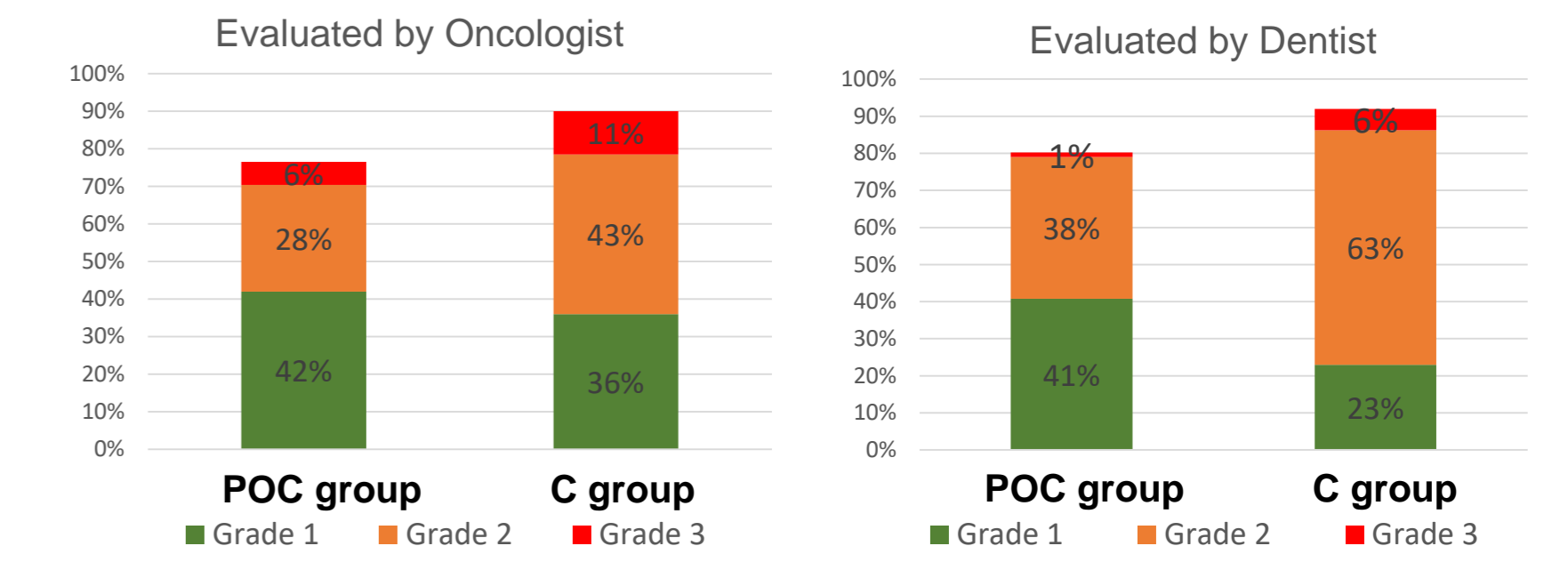
Incidence Probability of Oral Mucositis

	POC Group (n=81)		C Group (n=87)		P-value [†]
	n	%	n	%	
Oral Mucositis over Grade 1 (by Oncologist)					0.035
Yes	62	76.5	78	89.7	
No	19	23.5	9	10.3	
Risk Difference, % (95% CI)[†]	-11.83 (-22.80, -0.85)				
Chi-square Test					



	POC Group (n=81)		C Group (n=87)		P-value [†]
	n	%	n	%	
Oral Mucositis over Grade 2 (by Oncologist)					0.015
Yes	28	34.6	47	54.0	
No	53	65.4	40	46.0	
Risk Difference, % (95% CI)[†]	-18.75 (-33.53, -3.98)				
Oral Mucositis over Grade 3 (by Oncologist)					0.285
Yes	5	6.2	10	11.5	
No	76	93.8	77	88.5	
Risk Difference, % (95% CI)[†]	-4.77 (-13.41, 3.87)				
Oral Mucositis over Grade 1 (by Dental and Oral Surgeon)					0.033
Yes	65	80.2	80	92.0	
No	16	19.8	7	8.0	
Risk Difference, % (95% CI)[†]	-10.39 (-19.94, -0.83)				
Oral Mucositis over Grade 2 (by Dental and Oral Surgeon)					<0.001
Yes	32	39.5	60	69.0	
No	49	60.5	27	31.0	
Risk Difference, % (95% CI)[†]	-29.31 (-43.70, -14.92)				
Oral Mucositis over Grade 3 (by Dental and Oral Surgeon)					0.120
Yes	1	1.2	5	5.7	
No	80	98.8	82	94.3	
Risk Difference, % (95% CI)[†]	-4.49 (-10.00, 1.01)				

Incidence Probability of Oral Mucositis



Delay or Dose-Reduction of Everolimus

	POC Group (n=81)		C Group (n=87)		P-value [†]
	n	%	n	%	
Treatment delay					0.065
Yes	35	43.2	50	57.5	
No	46	56.8	37	42.5	
Risk Difference (95% CI)	-14.3 (-29.2, 0.7)				
Dose-Reduction of Everolimus Treatment due to Oral Mucositis					0.139
Yes	17	21.0	27	31.0	
No	64	79.0	60	69.0	
Risk Difference (95% CI)	-10.0 (-23.2, 3.1)				
Treatment delay or Dose Reduction					0.034
Yes	39	48.1	56	64.4	
No	42	51.9	31	35.6	
Risk Difference (95% CI)	-16.2 (-31.0, -1.4)				
Chi-square Test					

Conclusions

- Significantly fewer cases of grade 1 and 2 oral mucositis were observed in the POC group.
- No statistical difference in suspension or dose-reduction of everolimus between the POC and C groups.
- This study clearly demonstrated that the occurrence of oral mucositis were reduced by professional oral care prior to everolimus treatment.
- Professional oral care should be considered as a new standard treatment to prevent oral mucositis prior to everolimus treatment.

Acknowledgement

To all of the patients who participated in Oral Care-BC and their families
To the investigators and research coordinators at the 258 institutions and CSPOR.
This study was funded by the Comprehensive Support Project for Oncology Research (CSPOR) of the Public Health Research Foundation. The research fund was provided to CSPOR by Novartis Pharma K. K.. Novartis Pharma K. K. took no part in this study other than providing information relevant to proper use of the study drug. All decisions concerning the planning, implementation, and publication of this study were made by the executive committee.