

Non-Intensive Chemotherapy in Elderly: Low-Efficacy ICT is Too Toxic and Targeted Therapy is Optimal

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Introduction

The options for the treatment of elderly AML patients include intensive therapy for “fit” patients and non-intensive therapy for “unfit” patients. Until recently, non-intensive therapy ranged from BSC to single-agent HMA and LDAC. With the emergence of new therapies, the question of how best to treat AML in older or less fit adults becomes increasingly relevant.

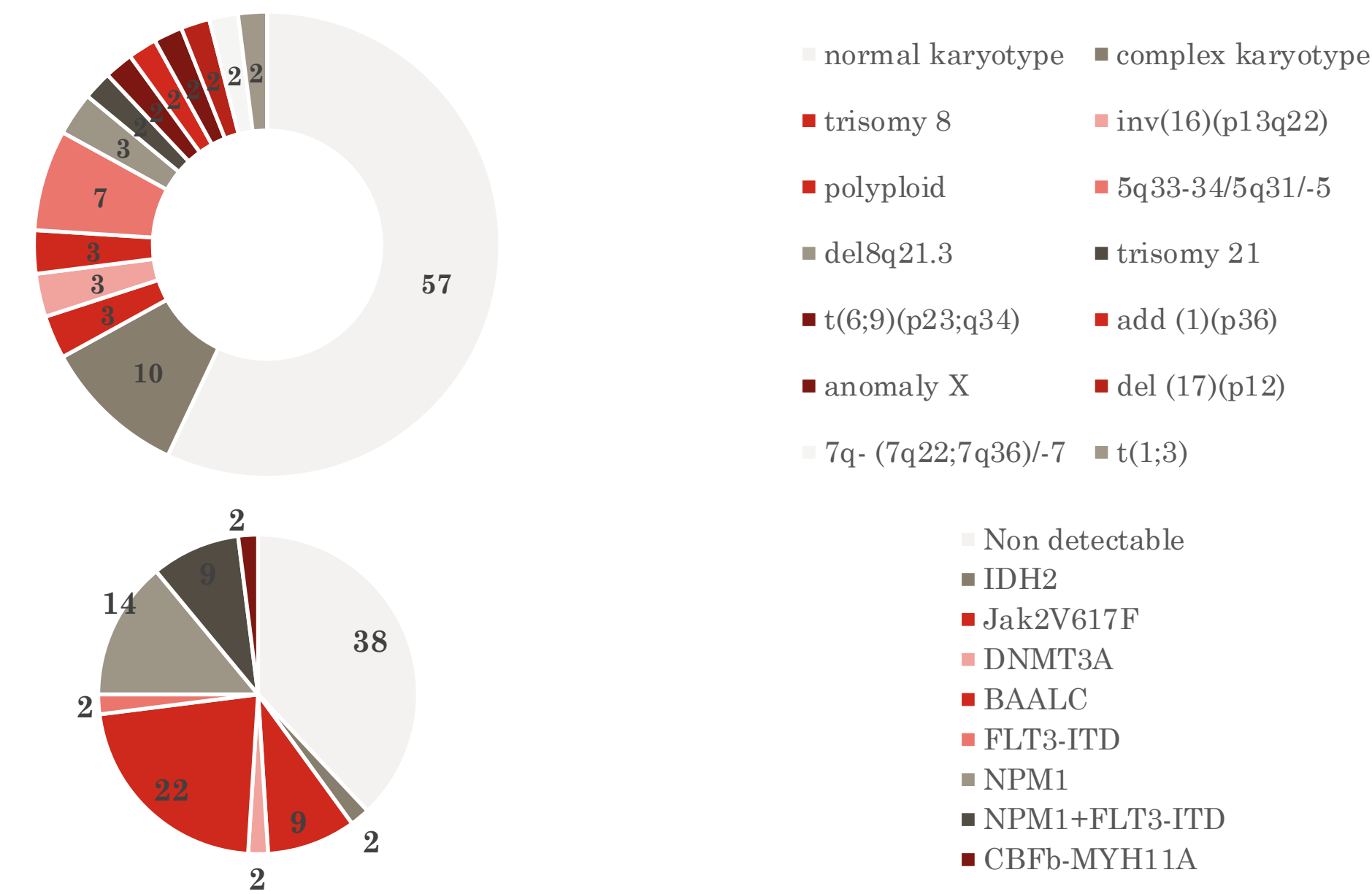
Objective

To determine whether less-intense therapy with new targets is as effective as ICT and as safe as non-intensive therapy.

Materials & Methods

40 previously untreated AML patients with a median age of 66 years (60–85) were included in this study. Patients were selected for intensive chemotherapy (n=17), less-intensive therapies, including LDAC or AZA alone (n=10) and combined with target agents (n=13: venetoclax, n=10; glasdegib, n=2; gemtuzumab ozogamicin, n=1). 37.5% of the patients had prior history of MDS/MPN (17.6% ICT, 50% AZA/AraC, 53% with target, p>0,05). According to the ELN classification, 15% were assigned as favorable, 55% as intermediate-risk, and 30% as adverse-risk.

Cytogenetic and molecular profile of patients



Patients Characteristics	
Total, n	40
Age, median years (range)	66 (60-85)
Cytogenic risk, ELN 2017	
favorable, n (%)	6 (15)
Intermediate, n (%)	22 (56,5)
Adverse, n (%)	12 (26,1)
De novo AML, n (%)	25 (62,5)
Post-MDS/CMML, n (%)	15 (37,5)

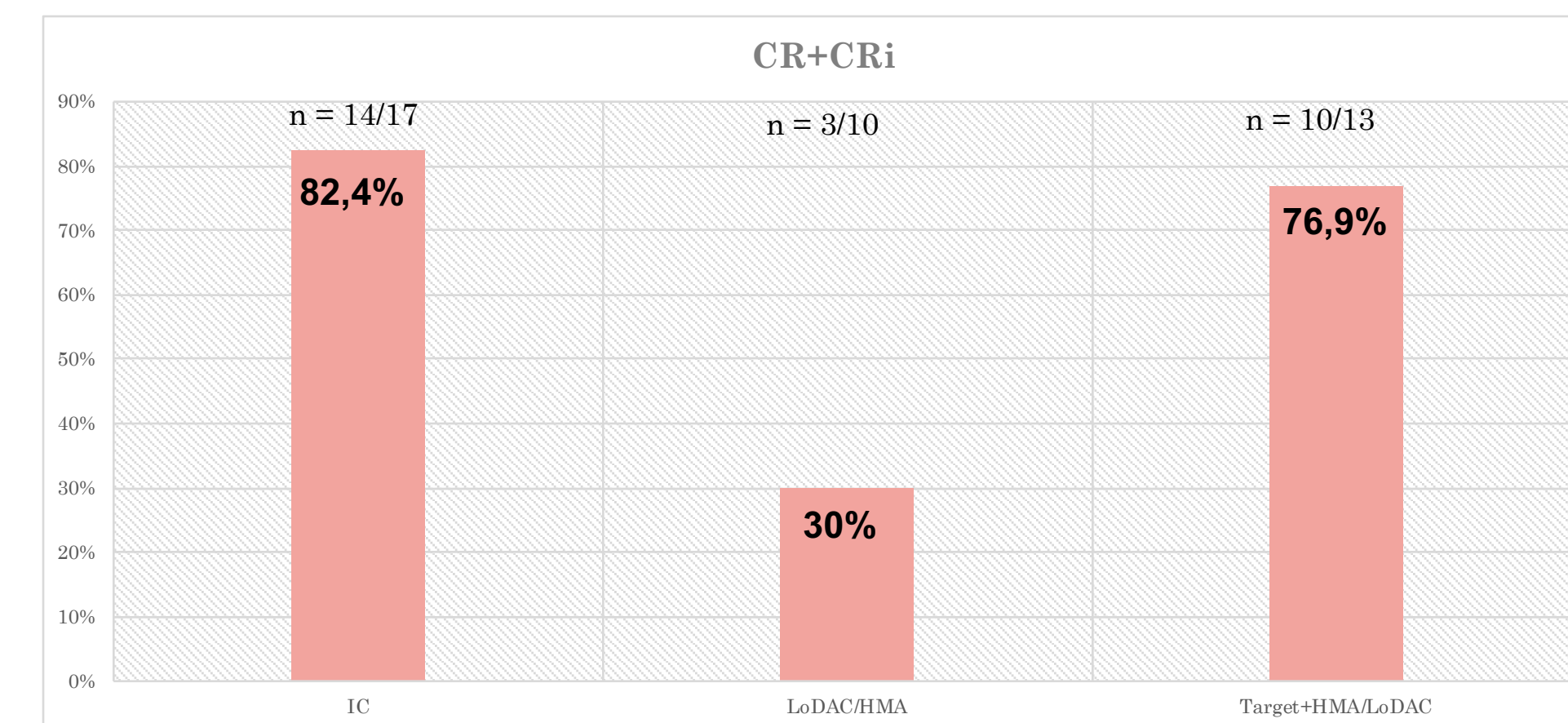
Median months (range)	IC	LoDAC/HMA	Target+HMA / LoDAC	p
Time to first response (CR or CRi), mo	1.0	2.9	1.2	0.002

AML=Acute Myeloid Leukemia. CR=Complete Remission. CRi=CR with Incomplete Blood Count Recovery. HMA=Hypomethylating Agent. LoDAC = Low-dose cytarabine. IC = Intensive therapy. BSC = Best supportive care. Non-IC – Non intensive therapy. OS=Overall Survival.

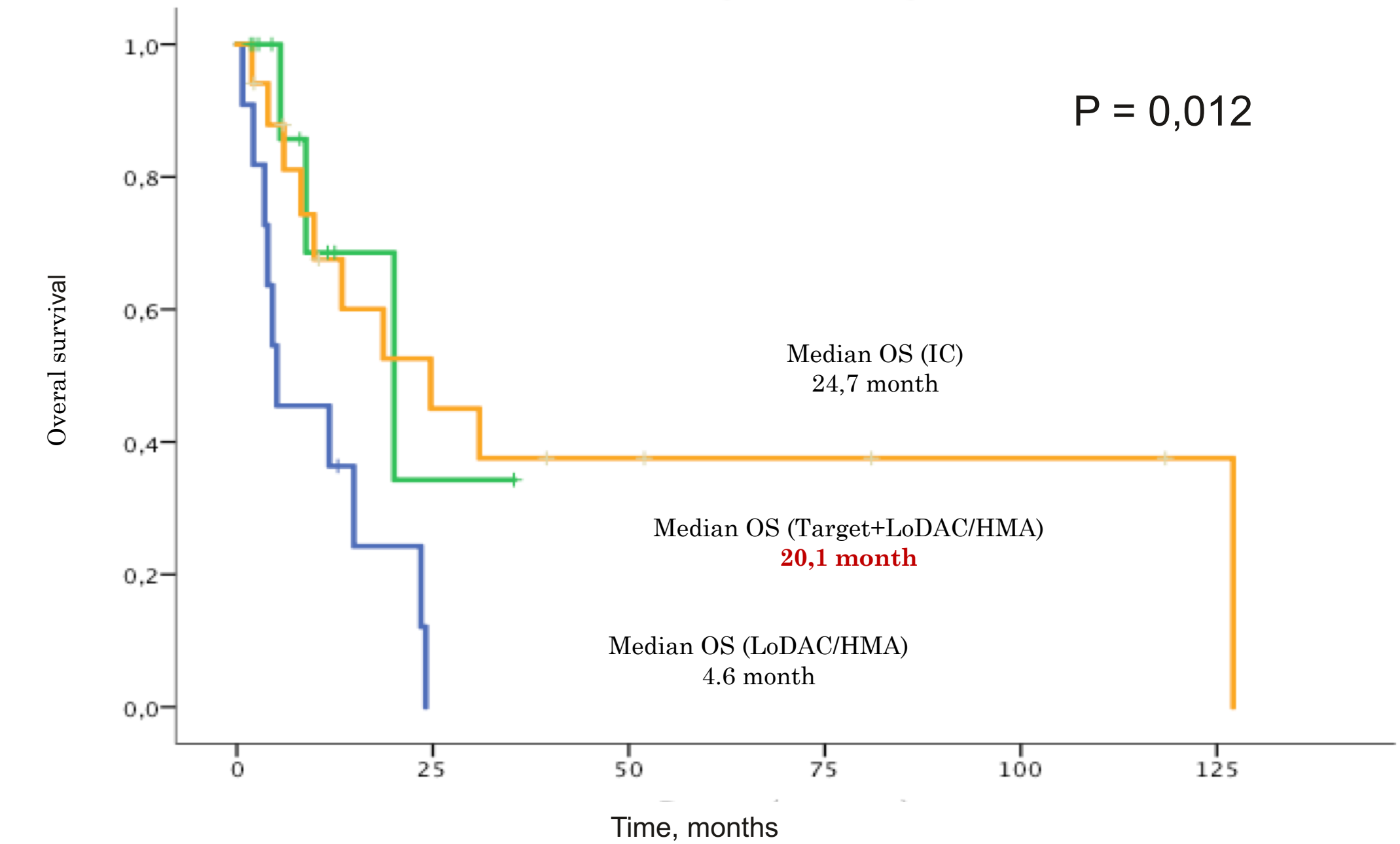
Results

The incidence of overall response (CR+CRi) was higher in the ICT and target groups than in the AZA/AraC group (82.4% vs. 76,9% vs. 30%; p=0.014). The median time to first response was 1.0 month (range: 0.8–2.0) in ICT, 1.2 months (range: 0.9–4.1) in the AZA/AraC+target group, and 2.9 months in the AZA/AraC group (range: 1.6–6.2, p=0.002). Among patients in the intermediate- and high-risk groups, the response rates were also significantly higher in the ICT and target groups (78.8% vs. 90% vs. 22.2%; p=0.003). At a median follow-up of 12 months, the median OS was 24.7 months in the ICT group, 20.1 months in the group with target agent treatment, and 4.5 months in the AZA / AraC group (HR: 0.51; 95% CI :0.31–0.86;p=0.012)

The most commonly reported infection AEs in the ICT and target groups included febrile neutropenia (94.1% vs. 57.1%; p<0.05); sepsis (41.2% vs. 7.1%; p<0.05)



Median Overall Survival IC vs LoDAC/HMA vs Target +LoDAC/HMA



Summary

In previously untreated AML patients, OS was longer, and the incidence of remission was higher among patients who received a combination of new targeted drugs with non-intensive regimens than among those who received azacitidine or AraC alone and was comparable to the ICT group, which was more toxic. However, the incidence of infection AEs was higher in the ICT group than in the non-intensive group.