

# Results of COG ACNS0331: A Phase III Trial of Involved-Field Radiotherapy (IFRT) and Low Dose Craniospinal Irradiation (LDCSI) with Chemotherapy in Average-Risk Medulloblastoma: A Report from the Children's Oncology Group

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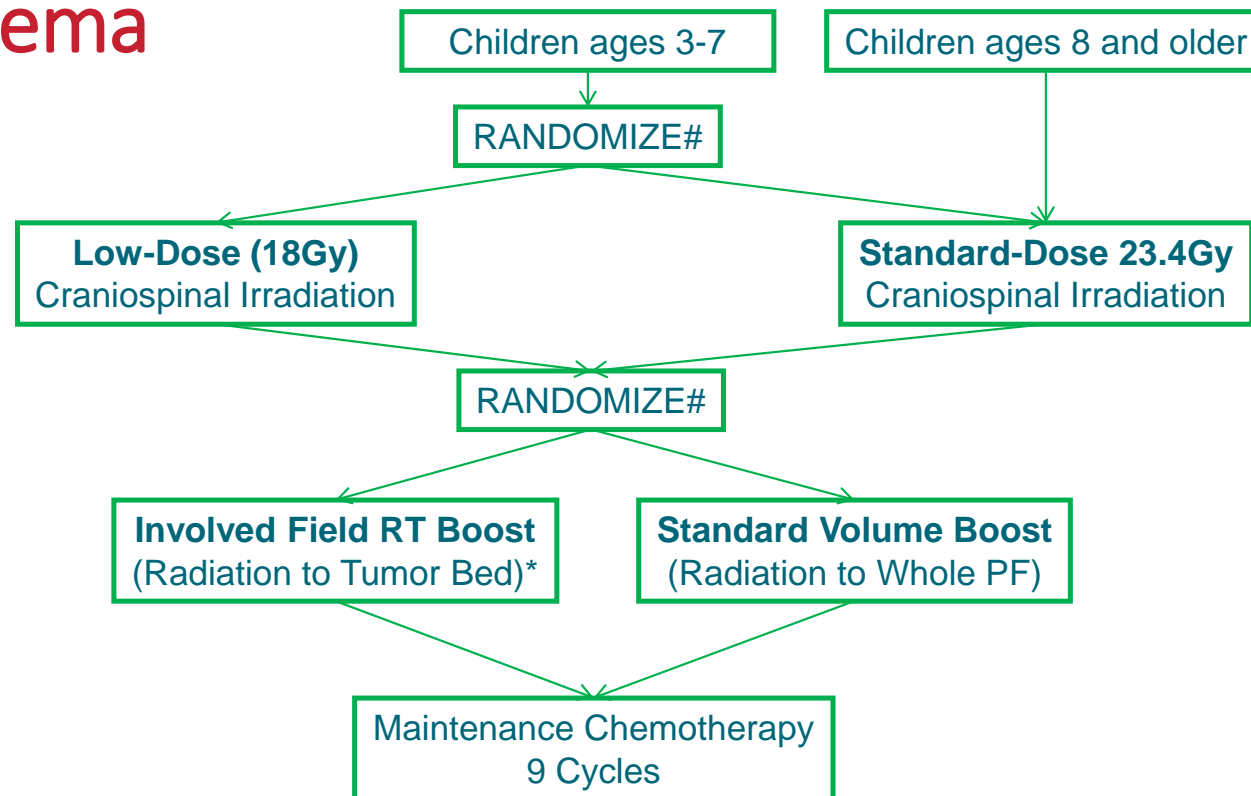
# Background

- Largest trial conducted for average-risk (A-R) medulloblastoma
  - Most common brain malignancy in children
  - Aggressive tumor with a propensity to spread from the lower brain to the upper brain and spine
- Current standard of care following surgical resection: systemic chemotherapy + irradiation to both primary site (posterior fossa) and craniospinal axis
  - Considerable negative effects on patients' neurocognitive abilities, endocrinologic function and hearing

## ACNS0331: Trial Objectives

- To determine if reducing the volume of the boost from the whole posterior fossa to the tumor bed will not compromise event-free and overall survival.
- To determine whether reducing the craniospinal dose of radiation therapy from 23.4 Gy to 18 Gy in children 3-7 years of age does not compromise event-free survival and overall survival
- Endpoints included Event Free Survival (EFS) and Overall Survival (OS)

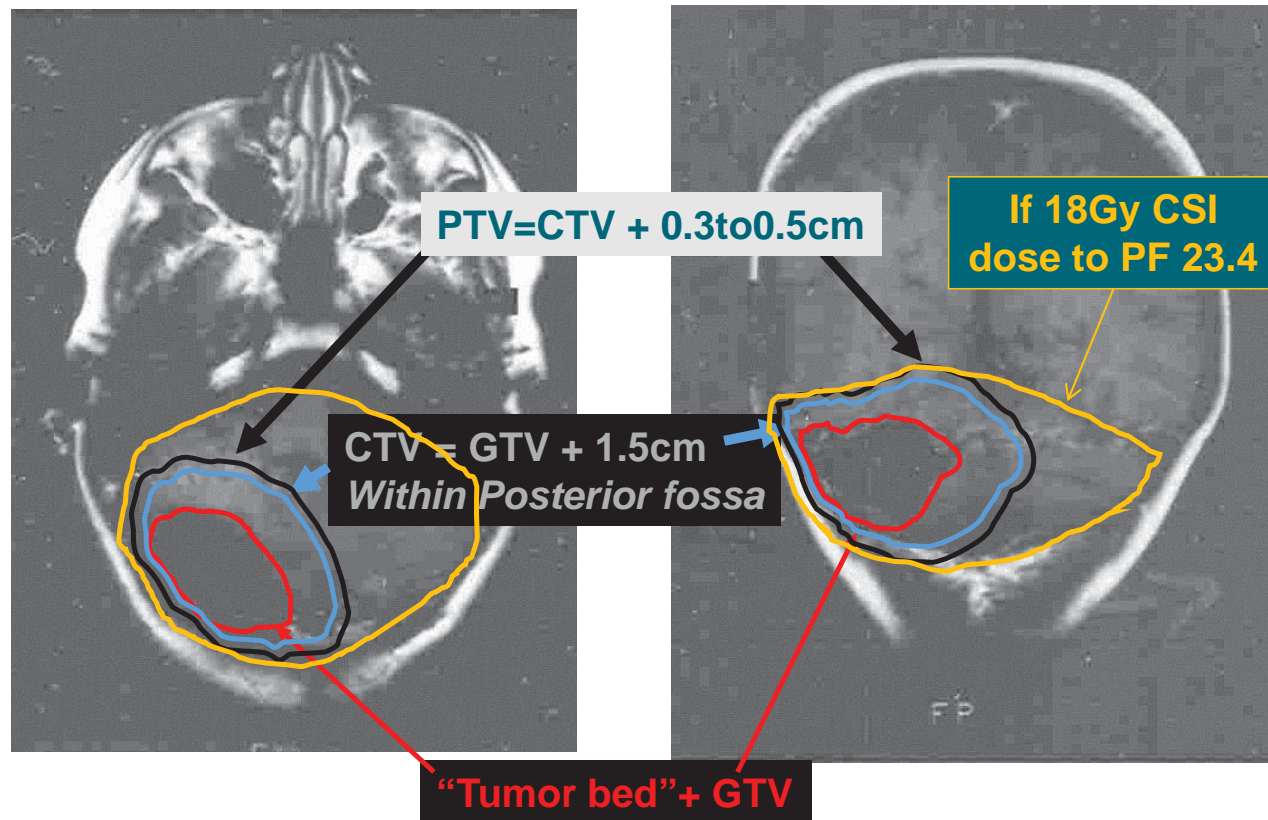
# Study Schema



\*Patients 3-7 randomized to reduced dose receive 5.4Gy to PF before IFRT

#Both randomizations occur at the time of study enrollment

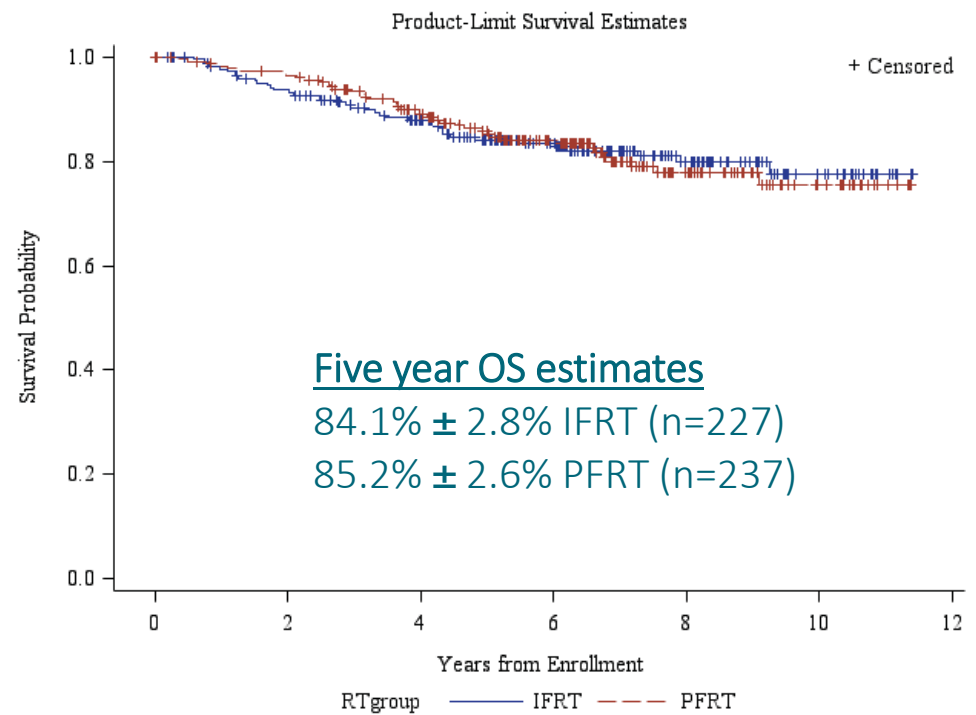
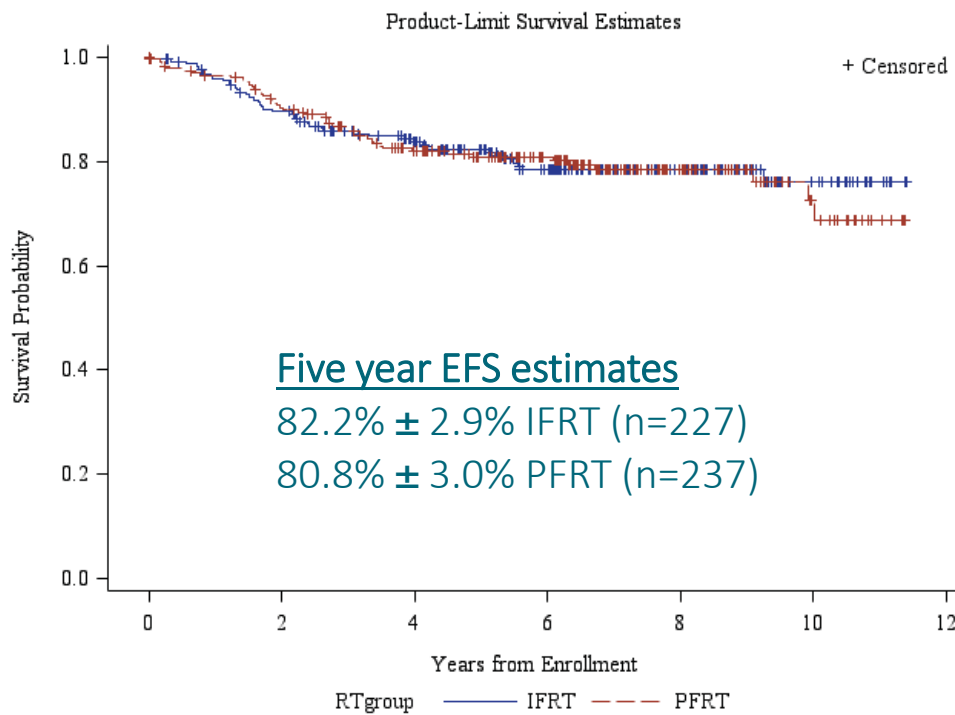
# Medulloblastoma Involved Field RT Boost of 54Gy



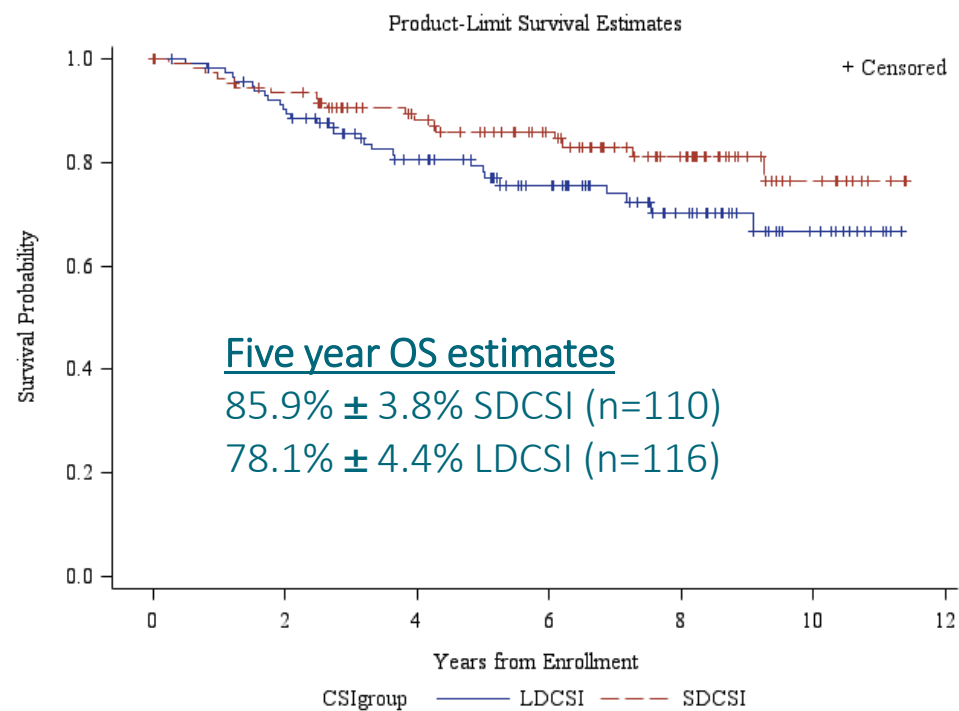
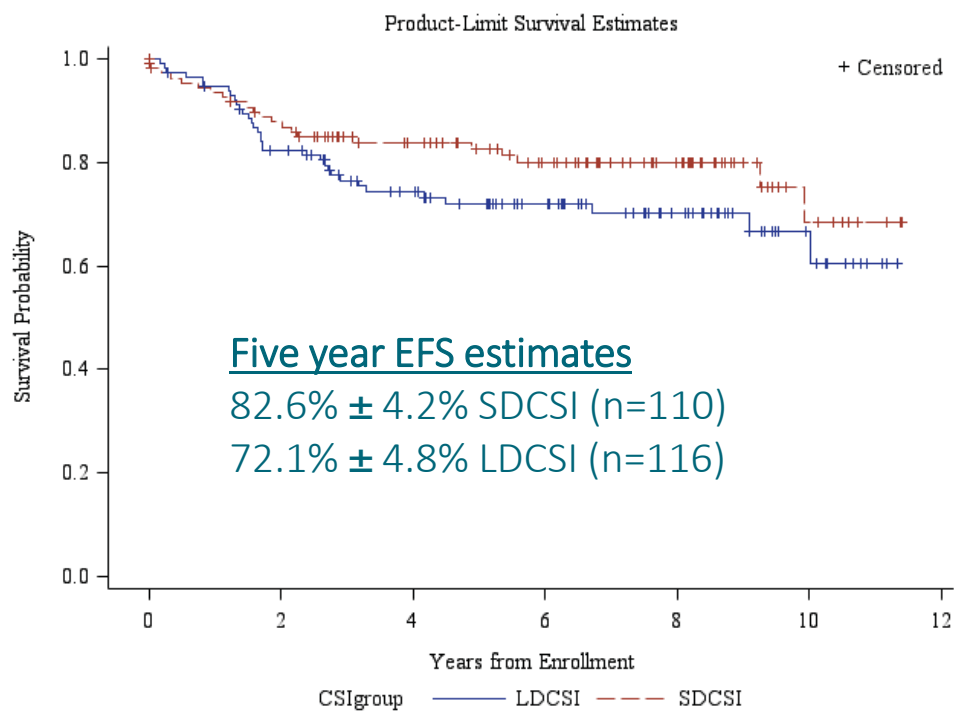
# Patient Characteristics

	All Patients n=513	All Patients		Patients 3-7 years of age	
		IFRT n=253	PFRT n=260	LDCSI n=127	SDCSI n=118
<b>Age on study (years)</b>					
Median	8.3	8.2	8.3	5.9	5.6
Range	3.0 – 21.8	3.0 – 19.8	3.1 – 21.8	3.2 – 7.9	3.0 – 8.0
<b>Sex</b>					
Male	329 (64%)	164 (65%)	165 (63%)	91 (72%)	74 (63%)
Female	184 (36%)	89 (35%)	95 (37%)	36 (28%)	44 (37%)
<b>Race</b>					
White	420 (82%)	204 (81%)	216 (83%)	98 (77%)	94 (80%)
Black or African American	41 (8%)	23 (9%)	18 (7%)	11 (9%)	8 (7%)
Asian	10 (2%)	6 (2%)	4 (2%)	0 (0%)	4 (3%)
Native Hawaiian or Other Pacific Islander	5 (1%) 2 (0.4%)	2 (1%) 2 (1%)	3 (1%) 0 (0%)	2 (2%) 0 (0%)	3 (3%) 1 (1%)
American Indian or Alaska Native	35 (7%)	16 (6%)	19 (7%)	16 (13%)	8 (7%)
Unknown					

# Results: Primary Site Irradiation



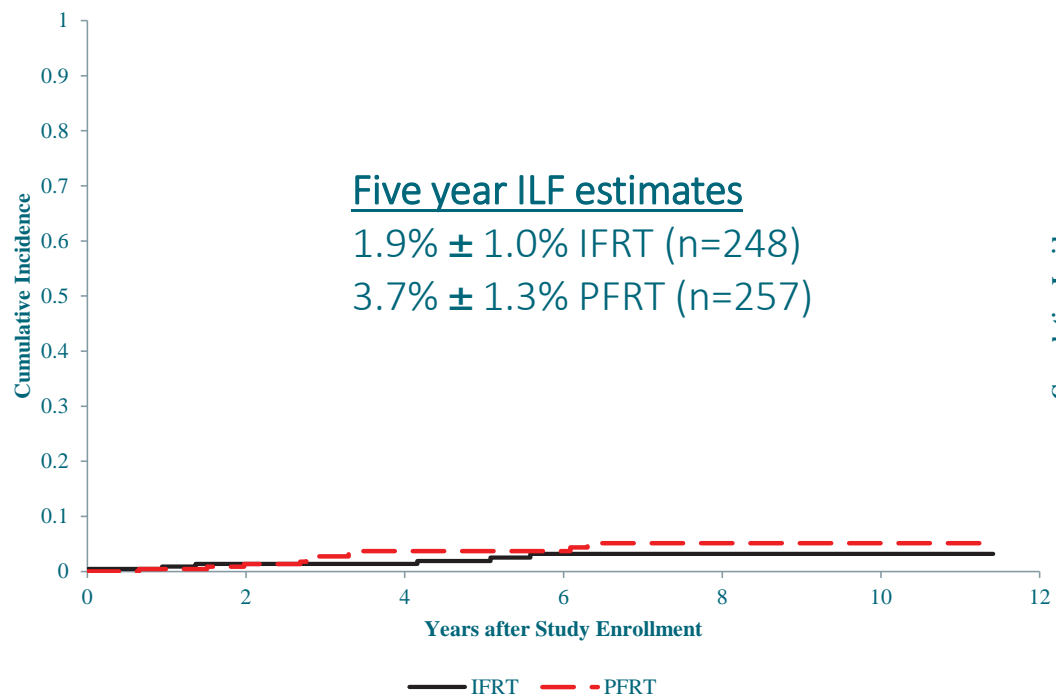
# Results: Craniospinal Irradiation



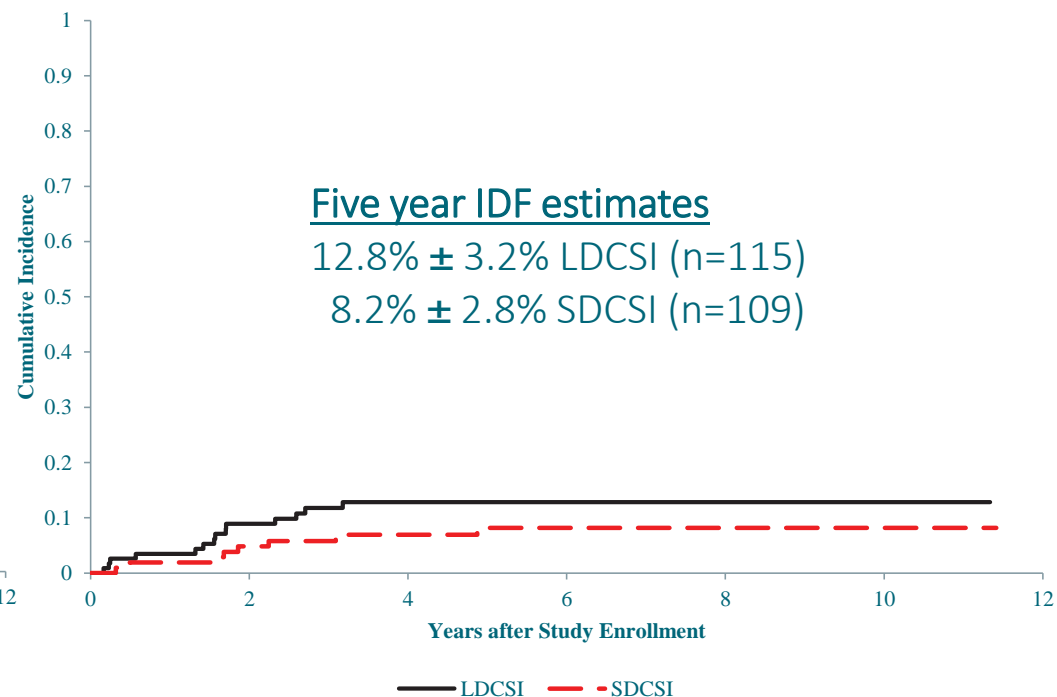


# Results: Local and Distant Failure

Cumulative Incidence of Local Failure for Eligible and Evaluable ACNS0331 Patients by RT Group



Cumulative Incidence of Distant Failure for Eligible and Evaluable ACNS0331 Patients 3 to 7 Years of Age by CSI Group



# Conclusions

- Survival rates following reduced radiation boost volumes were comparable to standard treatment volumes for the primary tumor site
  - First trial sufficiently powered to state definitively that there is no survival difference between the two approaches
- Reduced dose of craniospinal axis irradiation was associated with higher event rates and worse survival
- Physicians can adopt smaller boost volumes for posterior fossa RT but should maintain the standard RT dose for craniospinal irradiation