ASCO® Genitourinary Cancers Symposium

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Outcomes of patients with brain metastases from renal cell carcinoma treated with first-line therapies

Results from the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC)

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Overview of brain metastases from renal cell carcinoma (RCC)

- Incidence of RCC brain metastases is not well known in the era of immuno-oncology (IO) combinations
- Brain metastases confer poor overall survival (OS)
- Clinical effectiveness of 1L IO-based combinations in patients with RCC brain metastases needs to be evaluated because of frequent exclusion from trials

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Key clinical questions

1. Incidence of RCC brain metastases at first-line (1L) therapy initiation
2. Outcomes and prognostic factors in patients with RCC brain metastases
3. Temporal trends in brain-directed therapies for RCC brain metastases

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Methods

- Using the IMDC, a large, multinational cohort, patients with metastatic RCC who received any of the following 1L therapy regimens were included:
  - IO-based: NIVO/IPI, PEMB/AXI, AVEL/AXI, NIVO/CAB, PEMB/LENVA, or ATEZ/BEV
  - TKI: SUN or PAZ

- Comparison was made between contemporary IO-based combination therapy *vs.* traditional tyrosine kinase inhibitor (TKI) monotherapy

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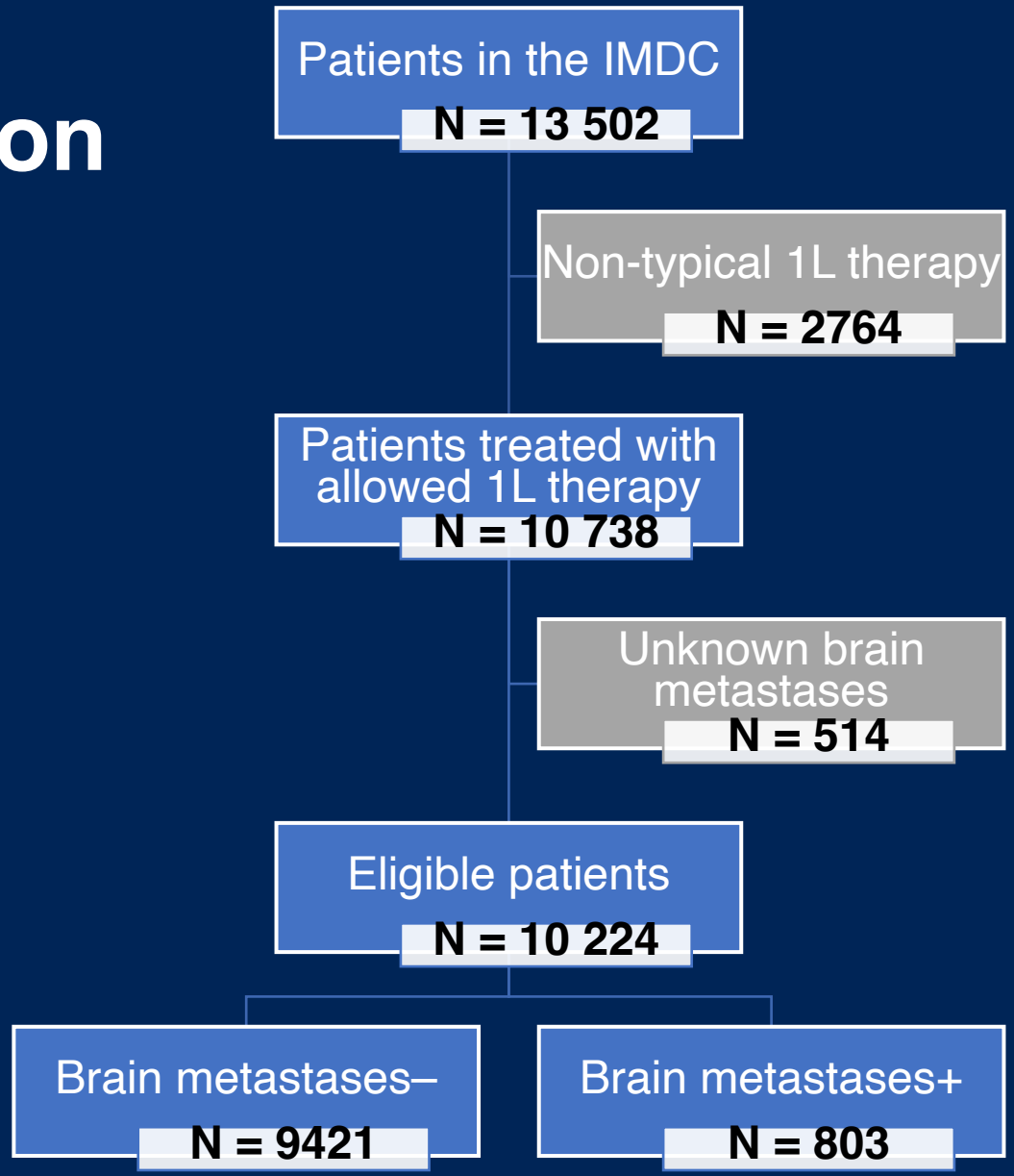
Cohort creation



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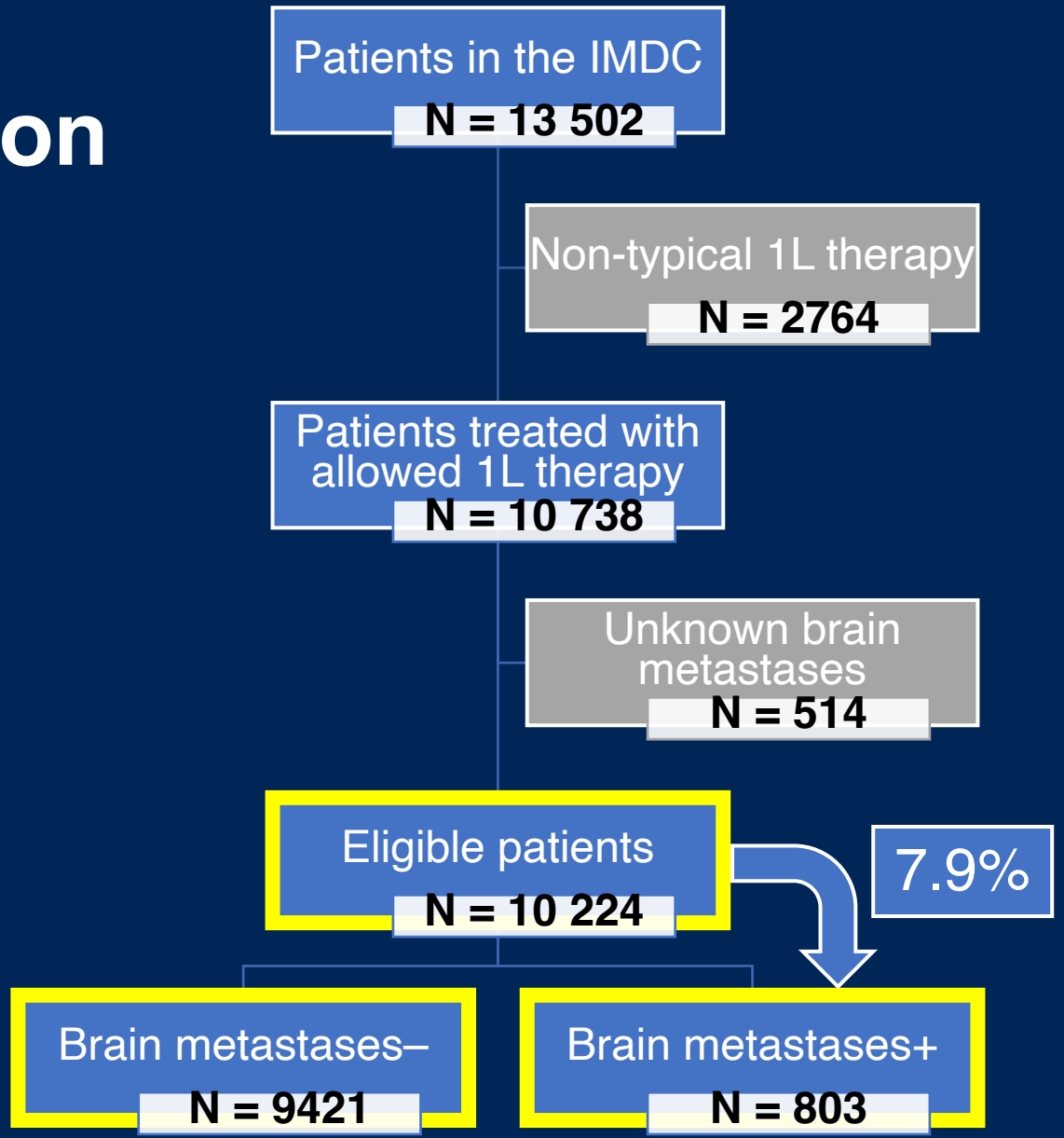
Cohort creation



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Characteristics of patients based on RCC brain metastases

Variable, N (%)	Brain metastases– (N = 9421)		Brain metastases+ (N = 803)		*P*
Age, median (IQR)	**64**	**(56–72)**	**62**	**(55–69)**	**< 0.001**
IMDC risk					**0.006**
Favourable	1378/7591	(18%)	93/640	(15%)	
Intermediate	4202/7591	(55%)	345/640	(54%)	
Poor	2011/7591	(26%)	202/640	(32%)	
1L regimens					0.103
IO-based	1364/9421	(14%)	99/803	(12%)	
TKI	8057/9421	(86%)	704/803	(88%)	

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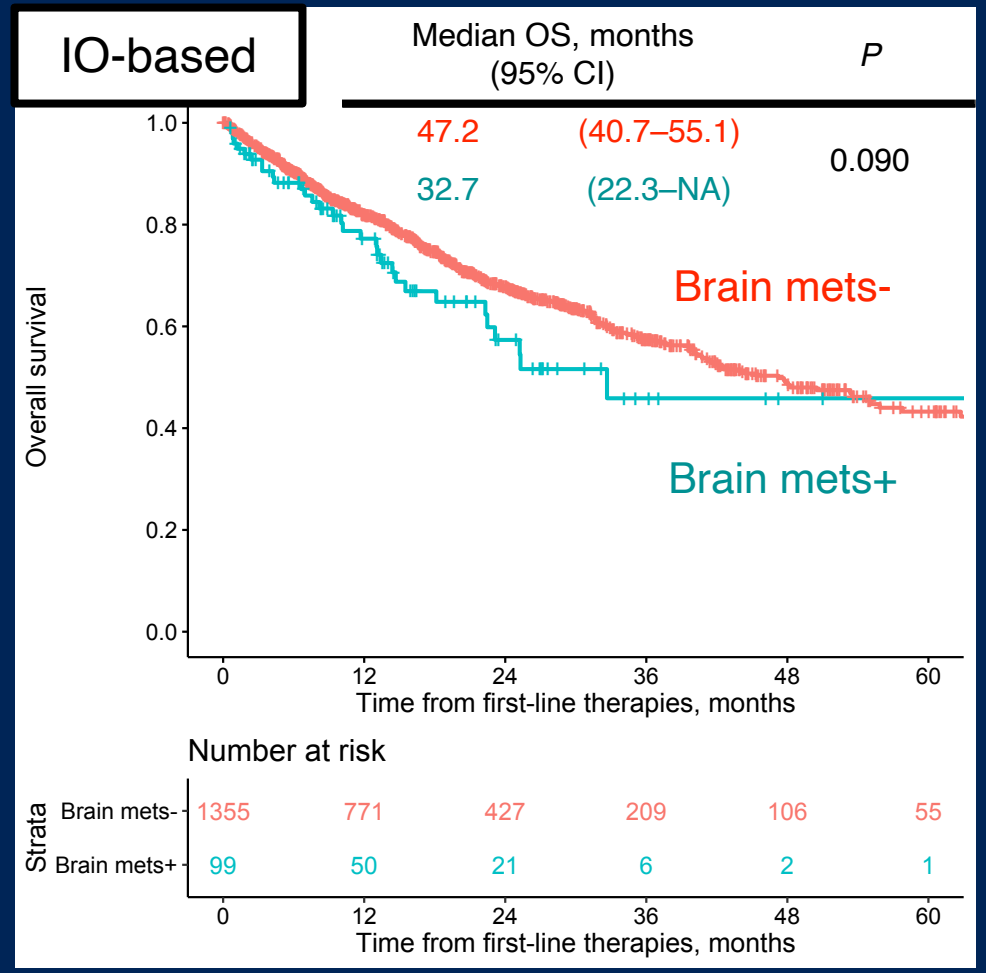
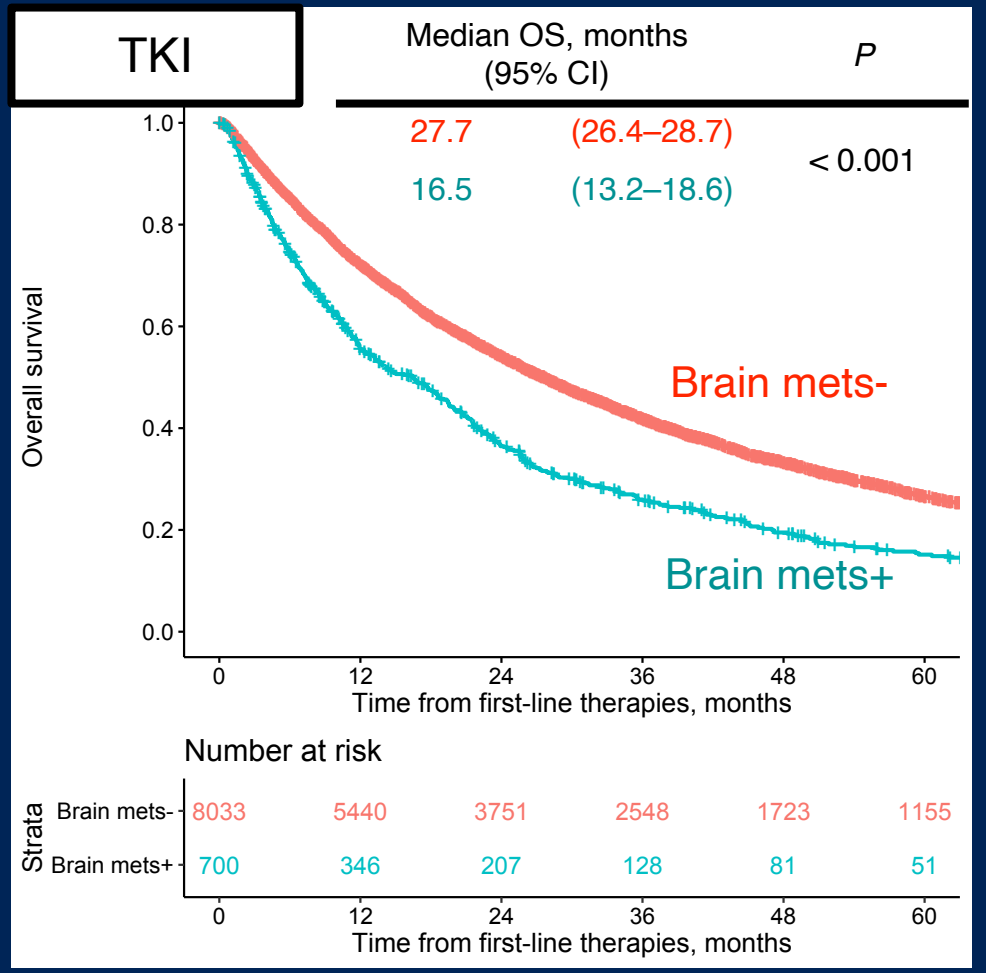
KM curves for OS in patients based on RCC brain metastases





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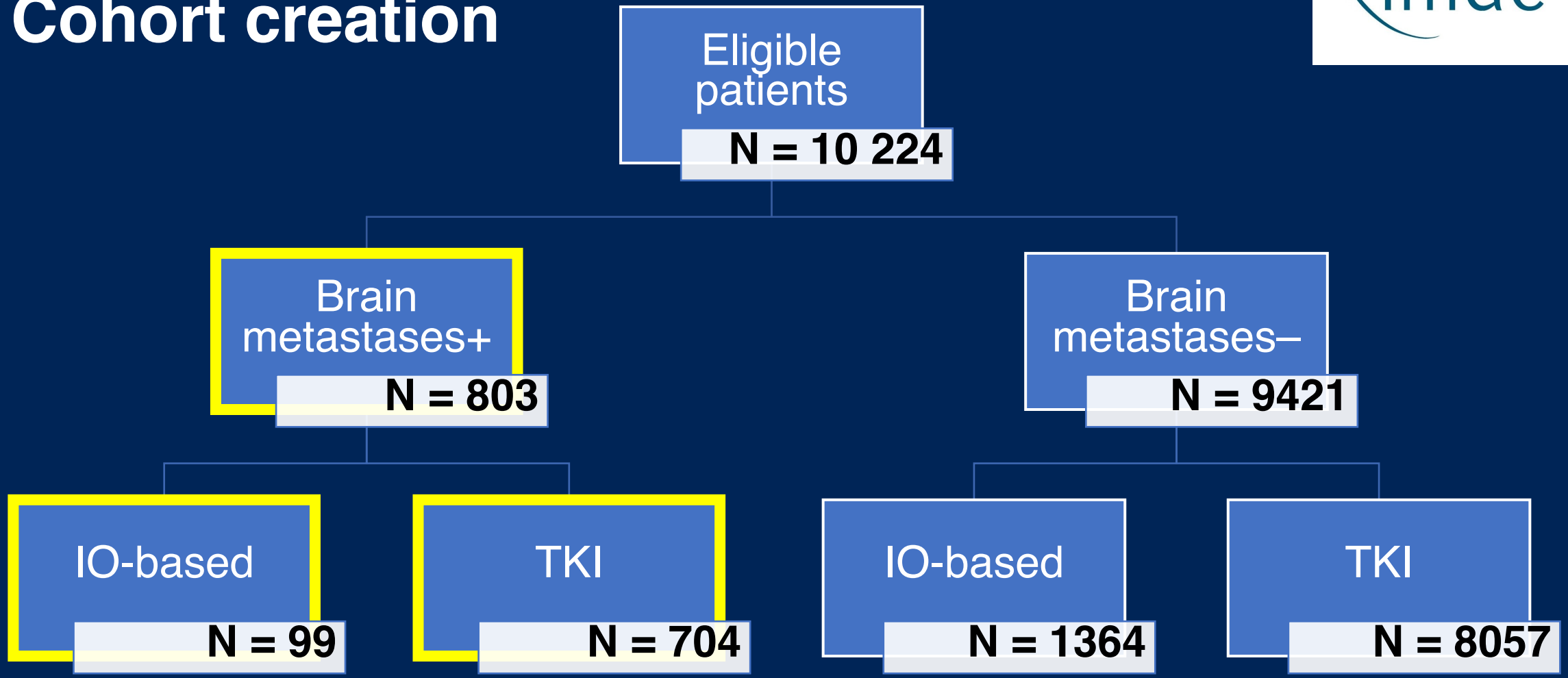
Cohort creation



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1L therapy regimens in patients with RCC brain metastases

IO-based cohort (N = 99)			TKI cohort (N = 704)		
NIVO/IPI	**80/99**	**(81%)**	**SUN**	**534/704**	**(76%)**
PEMB/AXI	9/99	(9%)	PAZ	170/704	(24%)
AVEL/AXI	2/99	(2%)			
NIVO/CAB	3/99	(3%)			
PEMB/LENVA	1/99	(1%)			
ATEZ/BEV	4/99	(4%)			

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Characteristics of patients based on 1L therapies (IO-based *vs.* TKI)

Variable, N (%)	IO-based cohort (N = 99)		TKI cohort (N = 704)		*P*
Age, median (IQR)	63	(56–69)	62	(55–69)	0.673
Year of 1L therapy ≥ 2014	**99/99**	**(100%)**	**290/704**	**(41%)**	**< 0.001**
IMDC risk					**0.033**
Favourable	9/84	(11%)	84/556	(15%)	
Intermediate	38/84	(45%)	307/556	(55%)	
Poor	37/84	(44%)	165/556	(30%)	
Symptoms at presentation	**34/60**	**(57%)**	**268/372**	**(72%)**	**0.022**
Multiple brain metastases	36/67	(54%)	201/386	(52%)	0.895
Whole-brain radiotherapy	**13/65**	**(20%)**	**232/476**	**(49%)**	**< 0.001**
Stereotactic radiosurgery	39/65	(60%)	224/476	(47%)	0.063
Neurosurgery	24/65	(37%)	135/476	(28%)	0.191

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Treatment response to 1L therapies (IO-based *vs.* TKI)

Best overall response, N (%)	IO-based cohort		TKI cohort	
Objective response*	**31/76**	**(41%)**	**181/586**	**(31%)**
Complete response	5/76	(7%)	4/586	(1%)
Partial response	26/76	(34%)	177/586	(30%)
Stable disease	25/76	(33%)	211/586	(36%)
Progressive disease	20/76	(26%)	194/586	(33%)

*$P = 0.090$

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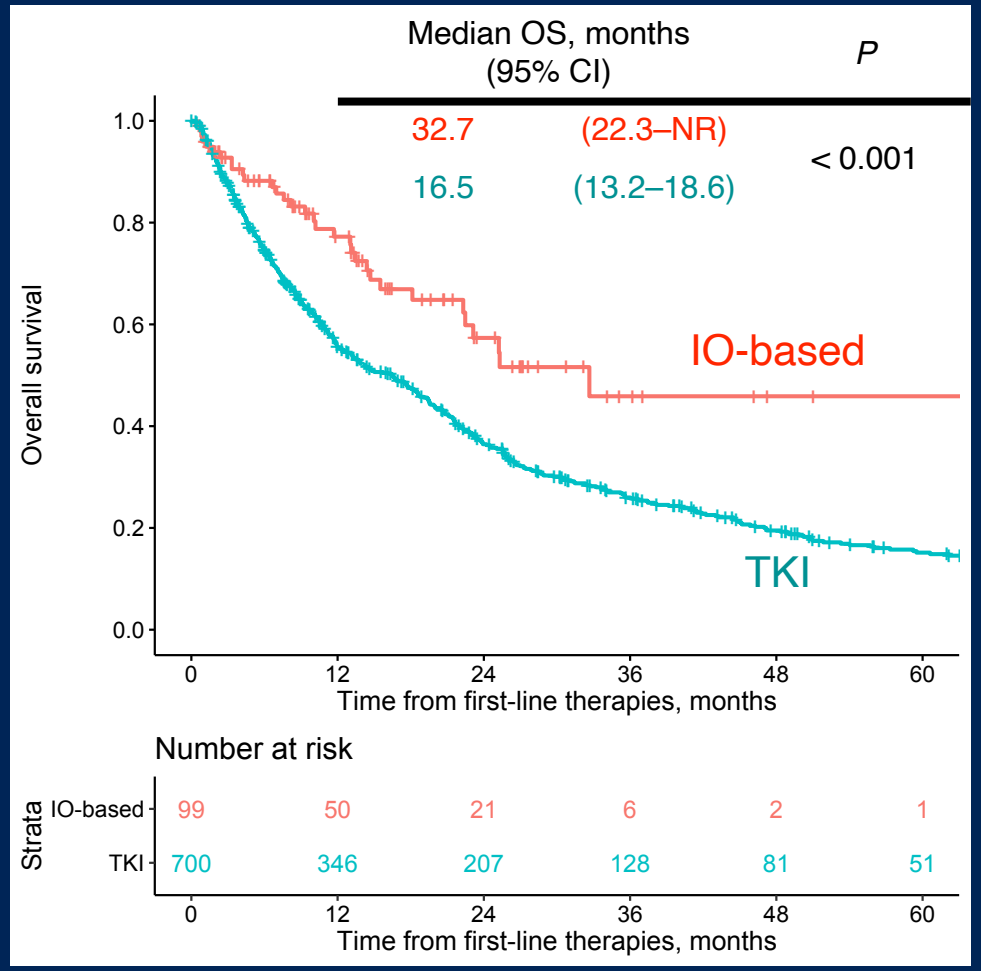
KM curves for OS in patients based on 1L therapies (IO-based *vs.* TKI)



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Multivariable analysis for OS in patients with RCC brain metastases

Variable	Adjusted HR	(95% CI)	*P*
1L therapy (IO-based *vs.* TKI)	**0.36**	**(0.21–0.61)**	**< 0.001**
Year of 1L therapy (≥ 2014 *vs.* < 2014)	0.92	(0.70–1.22)	0.581
IMDC risk (Fav/Int *vs.* Poor)	**0.43**	**(0.33–0.56)**	**< 0.001**
Symptoms at presentation	1.25	(0.95–1.65)	0.116
Multiple brain metastases	1.17	(0.90–1.52)	0.243
Whole-brain radiotherapy (WBRT)	1.01	(0.73–1.38)	0.971
Stereotactic radiosurgery (SRS)	**0.59**	**(0.44–0.79)**	**< 0.001**
Neurosurgery (NS)	**0.60**	**(0.45–0.81)**	**< 0.001**

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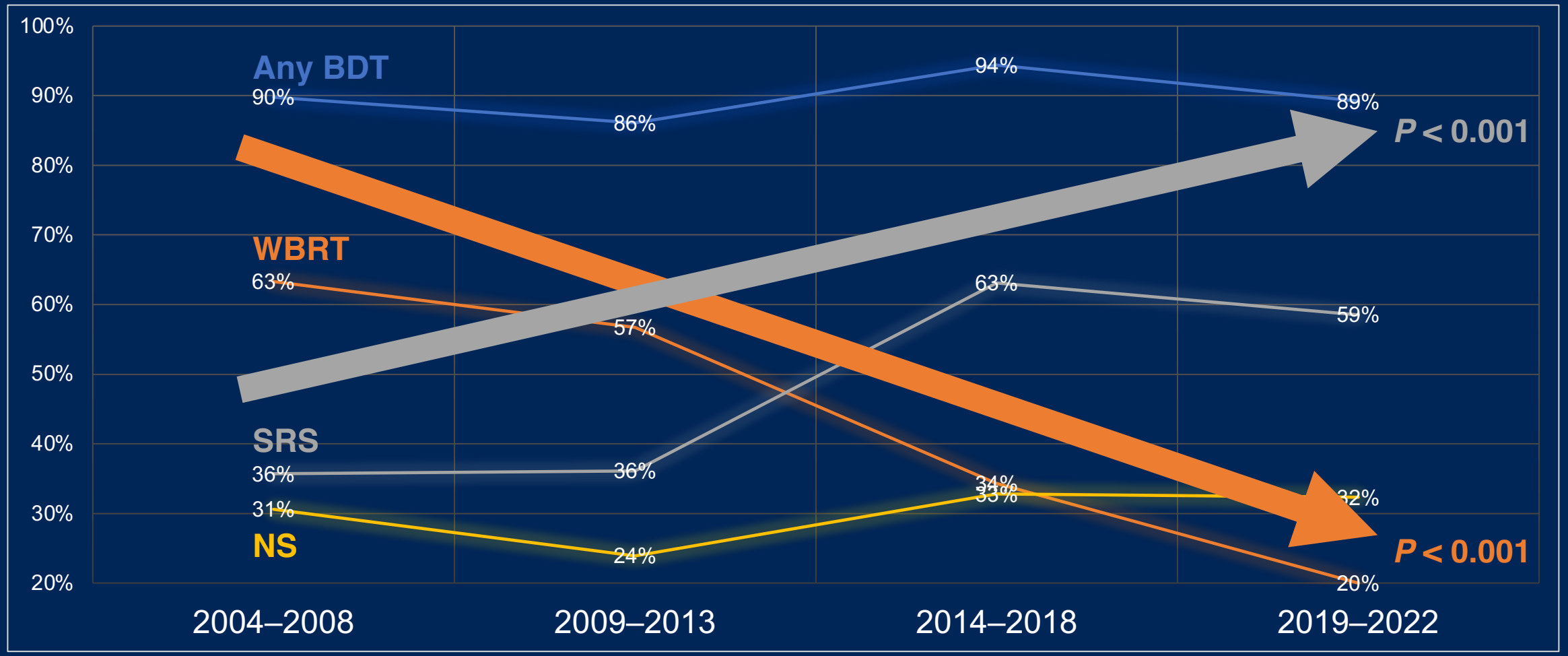
Proportions of brain-directed therapies



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Characteristics of patients based on brain-directed therapies

Variable, N (%)	SRS/NS (N = 343)		WBRT alone (N = 145)		No BDT (N = 53)		*P*
Age, median (IQR)	61	(54–67)	61	(54–70)	64	(58–70)	0.125
1L IO-based therapy	**48/343**	**(14%)**	**9/145**	**(6%)**	**8/53**	**(15%)**	**0.031**
Year of 1L therapy ≥ 2014	**198/343**	**(58%)**	**47/145**	**(32%)**	**18/53**	**(34%)**	**< 0.001**
IMDC risk							**0.001**
Favourable	47/287	(16%)	19/127	(15%)	4/43	(9%)	
Intermediate	167/287	(58%)	62/127	(49%)	15/43	(35%)	
Poor	73/287	(25%)	46/127	(36%)	24/43	(56%)	
Symptoms at presentation	**199/281**	**(71%)**	**83/110**	**(75%)**	**11/29**	**(38%)**	**< 0.001**
Multiple brain metastases	**133/295**	**(45%)**	**80/115**	**(70%)**	**17/30**	**(57%)**	**< 0.001**

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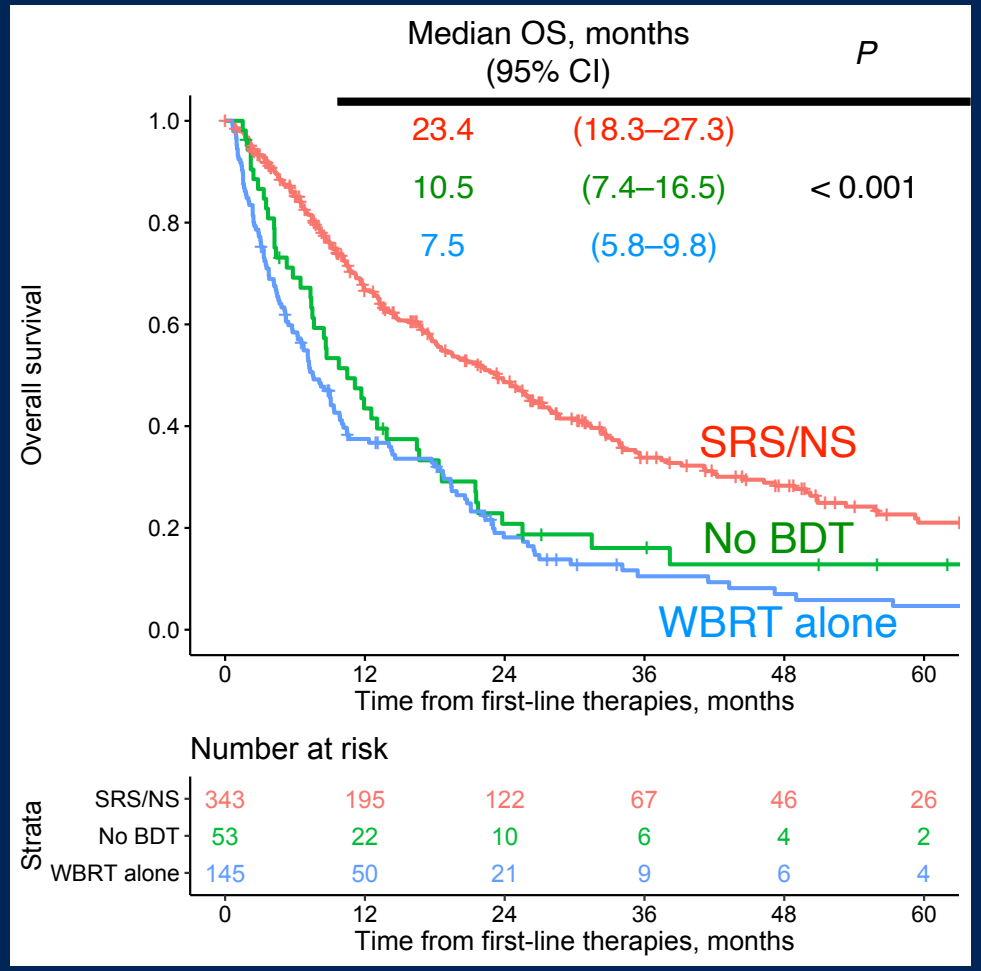
KM curves for OS in patients based on brain-directed therapies



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Conclusions

- Incidence of RCC brain metastases was 7.9% at 1L therapy initiation
- IO-based therapy and intensive brain-directed therapies were independently associated with longer OS in patients with RCC brain metastases
- There were changing practice patterns in brain-directed therapies
- Treatment of RCC brain metastases requires a multidisciplinary approach

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Acknowledgements

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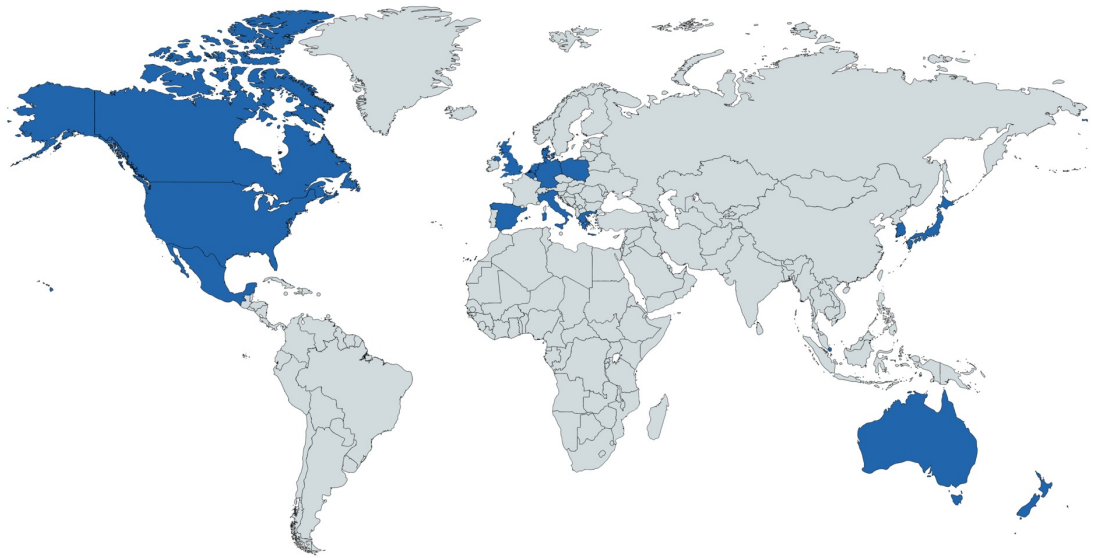

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