

# Intervention combining Nurse Navigators (NNs) and a mobile application vs. standard of care (SOC) in cancer patients (pts) treated with oral anticancer agents (OAA): results of CAPRI, a single-center, randomized phase 3 trial.

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# Background

- **Remote patient monitoring systems could improve patient follow-up and have a positive impact on quality of care, patient's experience and cost savings<sup>1,2</sup>**
- **Previously reported interventions aiming to improve a safe use of oral anti-cancer agents :**
  - Mostly retrospective studies
  - Restricted number of cancer types
- **Critical role for design phase prior to implementation**

⇒ *Need for prospective data*

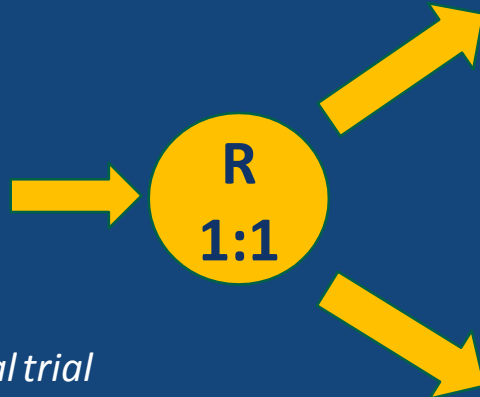
1: Denis et al, JAMA 2019; 2: Warrington et al, J Med Internet Res 2019

# Methods

- **Single center (tertiary cancer center), randomized phase 3 trial**
  - Intervention combining NNs + mobile application vs. standard of care
  - Duration of the intervention: 6 months
- **Key eligibility criteria :**
  - Adult patients with solid tumors
  - Oral treatment (excluding hormonal therapy)
  - PS < 3,
  - Life expectancy > 6 months
  - Access to phone and/or internet at home
  - Written informed consent

# Study design<sup>1</sup>

Adult cancer patients  
Advanced disease  
Approved oral treatment



Standard of care

**Nurse navigator (NN)**  
⇒ Weekly calls for 1 month then every other week  
⇒ Hotline Mon-Fri 09 AM – 05 PM

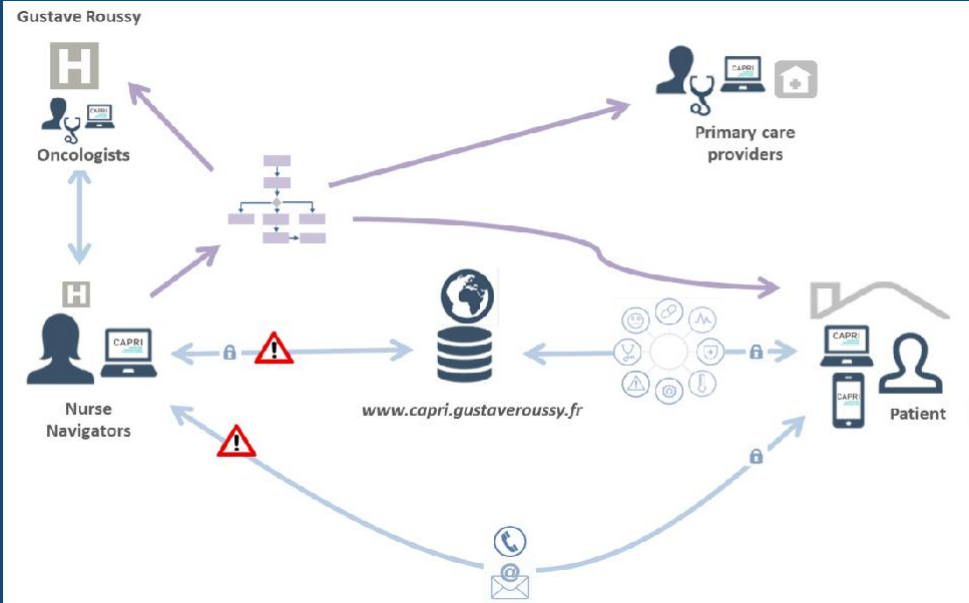
**Dedicated webiste / mobile application**  
80 algorithms => specific alerts

*for 6 months*

*Excluded: treatment in a clinical trial  
or compassionate use program,  
hormonal therapy alone*

**Web/mobile application**

- Dashboard for NNs to manage patients' records
- Interface for other healthcare professionals
- Patients can record tracking data, contact nurses via secure messaging, view therapy and side effect information or store documents



1: Gervès-Pinquié C et al, BMC Health Serv Res 2017

# Methods (continued)

- **Primary endpoint : Relative Dose Intensity (RDI) at 6 months**

- Hypothesis : increase by 5% (85 => 90%), two-sided  $\alpha = 0.05$ , power 80%
- Sample size estimation:  $n = 1000$  (800 + 200 lost to follow-up)
- Stratification: treatment line, treatment type (chemotherapy vs. molecular targeted therapy)

- **Secondary endpoints :**

- Adherence (Morisky questionnaire, electronic medication monitoring system)
- Grade  $\geq 3$  toxicity (NCI-CTCAE 4.03) <sup>1</sup>
- Patients' experience (PACIC score: visit 6)<sup>2</sup>
- Quality of life (EORTC QLQ-C30: visits 0, 3, 6)<sup>3</sup>
- Use of supportive care resources
- Economic estimation of the use of healthcare resources
- ORR (RECIST 1.1)<sup>4</sup>, PFS and OS

1: [ctep.cancer.gov](http://ctep.cancer.gov); 2: Glasgow et al, Med Care 2005; 3: Aaronson et al, JNCI 1993; 4: Eisenhauer et al, Eur J Cancer 2009

# Patient's characteristics (1)

From October 2016 to May 2019: 609 patients included, 559 evaluable (50 received < 28 days of treatment)  
Inclusions ended in May 2019 due to insufficient funding.

	CAPRI	CONTROL	Total
<b>N</b>	272	287	559
<b>Gender:</b>			
<b>Men</b>	116 (42.6%)	113 (39.4%)	229 (41.0%)
<b>Women</b>	156 (57.4%)	174 (60.6%)	330 (59.0%)
<b>Age (years) :</b>			
< 45	42 (15.4%)	37 (12.9%)	79 (14.1%)
45-54	45 (16.5%)	49 (17.1%)	94 (16.8%)
55-64	70 (25.7%)	83 (28.9%)	153 (27.4%)
65-74	76 (27.9%)	79 (27.5%)	155 (27.7%)
> 75	39 (14.3%)	39 (13.6%)	78 (14.0%)
<b>Oral chemotherapy</b>	109 (40.1%)	109 (38.0%)	218 (39.0%)
<b>Molecular targeted therapy</b>	162 (59.6%)	177 (61.7%)	339 (60.6%)
<i>incl. electronic medication monitoring</i>	62 (77.5%)	66 (75.0%)	128 (76.2%)

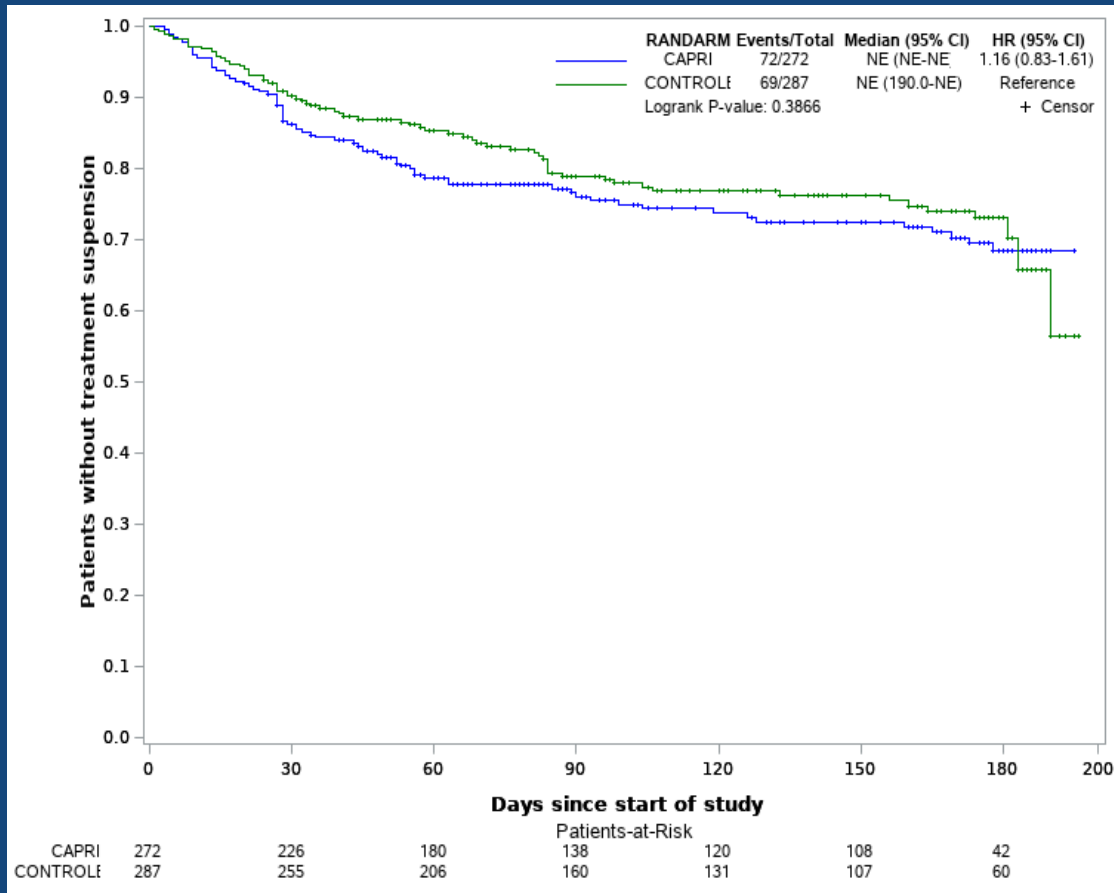
# Patient's characteristics (continued)

		CAPRI	CONTROL	Total
ECOG PS	0 - 1	241 (88.6%)	252 (87.9%)	492 (88.2%)
	2	31 (11.4%)	35 (12.2%)	66 (11.8%)
No. of previous treatment lines	0 - 1	143 (54.6%)	136 (51.1%)	279 (52.9%)
	2	48 (18.3%)	54 (20.3%)	102 (19.3%)
	>= 3	71 (27.1%)	76 (28.6%)	147 (27.8%)
Primary tumor site	Endocrine	51 (18.8%)	47 (16.4%)	98 (17.5%)
	Breast	48 (17.6%)	55 (19.2%)	103 (18.4%)
	Digestive	43 (15.8%)	48 (19.6%)	91 (16.3%)
	Renal	32 (11.8%)	32 (11.1%)	64 (11.4%)
	CNS	27 (9.9%)	26 (9.1%)	53 (9.5%)
	Sarcoma	21 (7.7%)	24 (8.4%)	45 (8.1%)
	Gynecological	15 (5.5%)	18 (6.2%)	33 (5.9%)
	Lung	14 (5.1%)	17 (5.9%)	31 (5.5%)
	Hematological	6 (2.2%)	6 (2.1%)	12 (2.1%)
	Melanoma	5 (1.8%)	4 (1.4%)	9 (1.6%)
	Other	2 (0.7%)	1 (0.3%)	3 (0.5%)

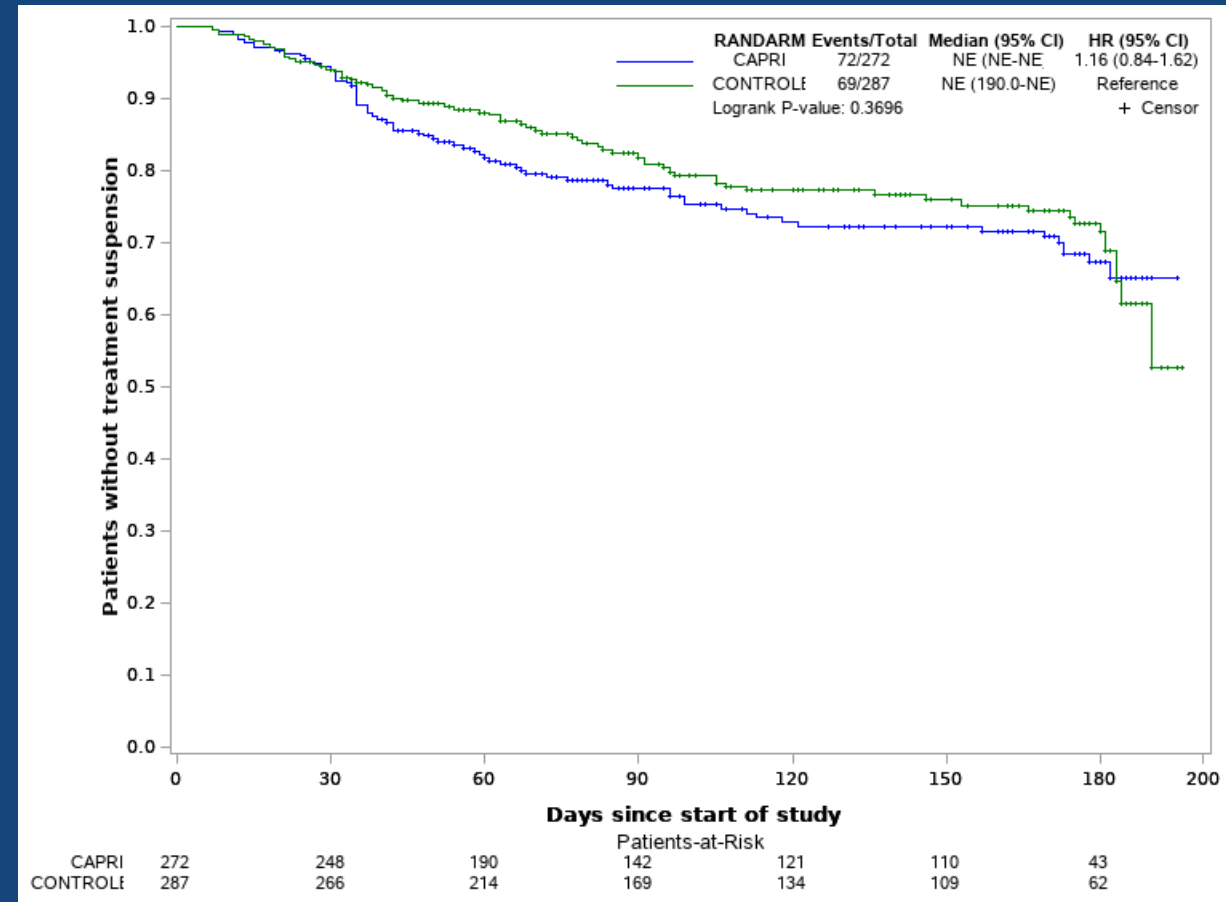
# Primary endpoint: relative dose-intensity

		CAPRI	CONTROL	Total	p-value
<b>RDI (until end of study)</b>	Missing	0	0	0	
	N	272	287	559	
	Mean (SD)	0.9344 (0.2590)	0.8943 (0.1914)	0.9138 (0.2275)	p = 0.0426
	95% CI	[0.9035 ; 0.9653]	[0.8720 ; 0.9165]	[0.8949 ; 0.9327]	
<b>RDI Adjusted on adherence (Morisky questionnaire)</b>	Missing	17 (6.3%)	22 (7.7%)	39 (7.0%)	
	N	255	265	520	
	Mean (SD)	0.8417 (0.2632)	0.7998 (0.2090)	0.8204 (0.2378)	p = 0.0451
	95% CI	[0.8093 ; 0.8742]	[0.7745 ; 0.8251]	[0.7999 ; 0.8408]	





Time to first treatment interruption due to toxicity



Time to treatment re-introduction after the first interruption due to toxicity

# Adherence

		CAPRI	CONTROL	Total	p-value
<b>Adherence - Morisky score</b>	Missing	17 (6.3%)	22 (7.7%)	39 (7.0%)	
	N	255	265	520	
	High/Medium	240 (94.1%)	239 (90.2%)	479 (92.1%)	p = 0.10
	Low	15 (5.9%)	26 (9.8%)	41 (7.9%)	
<b>Adherence - Monitoring system</b>	Missing	235 (86.4%)	248 (86.4%)	483 (86.4%)	
	N	37	39	76	
	Mean (SD)	94.7 (8.1)	95.2 (5.8)	95.0 (7.0)	p = 0.75
	95% CI	[92.0 ; 97.4]	[93.3 ; 97.1]	[93.4 ; 96.6]	

# Grade $\geq 3$ toxicities

(no grade 5 toxicity occurred)

		CAPRI	CONTROL	Total	p-value
	N	272	287	559	
<b>At least one toxicity grade <math>\geq 3</math></b>	No	197 (72.4%)	181 (63.1%)	378 (67.6%)	
	Yes	75 (27.6%)	106 (36.9%)	181 (32.4%)	p = 0.02
<b><i>Skin toxicities</i></b>	No	262 (96.3%)	265 (92.3%)	527 (94.3%)	
	Yes	10 (3.7%)	22 (7.7%)	32 (5.7%)	p = 0.04
<b><i>Metabolic /nutritional toxicities</i></b>	No	263 (96.7%)	266 (92.7%)	529 (94.6%)	
	Yes	9 (3.3%)	21 (7.3%)	30 (5.4%)	p = 0.04

# Hospitalizations

Variable		CAPRI	CONTROL	Total	p-value
	N	272	287	559	
Patients with at least one hospitalization	No	210 (77.2%)	196 (68.3%)	406 (72.6%)	p = 0.02
	Yes	62 (22.8%)	91 (31.7%)	153 (27.4%)	
	N	272	287	559	
Days of hospitalization / patient	Mean (SD)	2.82 (6.96)	4.44 (9.60)	3.65 (8.45)	p = 0.02
	95% CI	[1.99 ; 3.65]	[3.32 ; 5.55]	[2.95 ; 4.35]	
Patients with emergency hospitalizations	No	231 (84.9%)	224 (78.0%)	455 (81.4%)	p = 0.04
	Yes	41 (15.1%)	63 (22.0%)	104 (18.6%)	

# Use of supportive care resources (ambulatory)

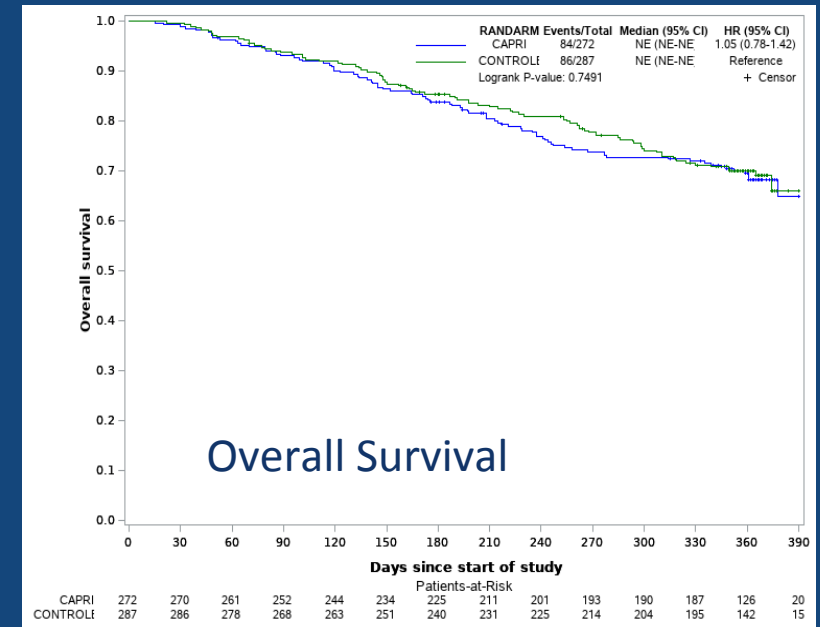
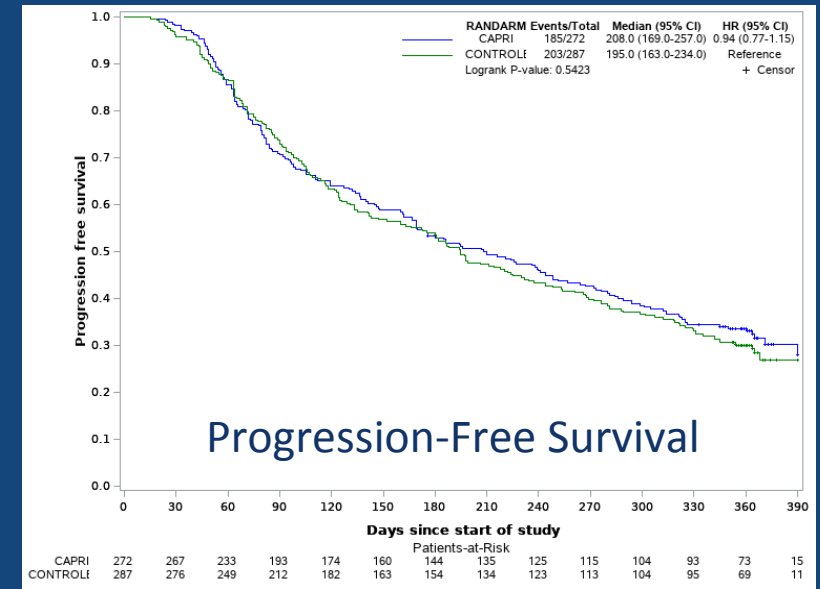
Variable		CAPRI	CONTROL	Total	p-value
Use of supportive care resources	N	272	287	559	
	No	153 (56.3%)	186 (64.8%)	339 (60.6%)	
	Yes	119 (43.8%)	101 (35.2%)	220 (39.4%)	p = 0.04
Type	Analgesia	10 (3.7%)	15 (5.2%)	25 (4.5%)	p = 0.38
	Nutrition	39 (14.3%)	25 (8.7%)	64 (11.4%)	p = 0.04
	Palliative care	17 (6.3%)	15 (5.2%)	32 (5.7%)	p = 0.60
	Psychologist	37 (13.6%)	41 (14.3%)	78 (14.0%)	p = 0.82
	Social worker	59 (21.7%)	31 (10.8%)	90 (16.1%)	p = 0.0005
	Other	14 (5.1%)	24 (8.4%)	38 (6.8%)	p = 0.13

# Patient's experience and Quality of life

		CAPRI	CONTROL	TOTAL	
<b>PACIC global score</b>	N	124	121	245	
	Mean (SD)	2.94 (0.83)	2.67 (0.89)	2.81 (0.87)	p = 0.01
	95% CI	[2.80; 3.09]	[2.51; 2.83]	[2.70; 2.92]	
<b>Global QoL (QLQ-C30)</b>	Missing	72 (26.5%)	93 (32.4%)	165 (29.5%)	
	N	200	194	394	p = 0.23
	Mean (SD)	-6.8 (22.9)	-4.0 (24.1)	-5.4 (23.5)	
	95% CI	[-10.0; -3.6]	[-7.4; -0.6]	[-7.8; -3.1]	

# Response and survival

Best response at 6 months		CAPRI	CONTROL	TOTAL	
Missing		41 (15.1%)	31 (10.8%)	72 (12.9%)	X = 1.42
N		231	256	487	p = 0.23
Non-progression		136 (58.9%)	137 (53.5%)	273 (56.1%)	
Progression		95 (41.1%)	119 (46.5%)	214 (43.9%)	



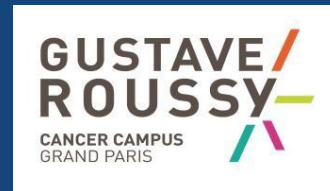
# Discussion

- **The analysis is based on 559 patients instead of 800**
  - ⇒ Secondary endpoints and subgroups could not be fully explored (ORR and survival)
- **External validity ?**
  - ⇒ Prospective, randomized design
  - ⇒ Tertiary cancer center but real-life population (14.0% aged > 75, 11.8% PS 2)
  - ⇒ Critical role of algorithms used by NNs
- **Future studies dedicated to adherence, specific tumor types and specific drug classes are planned**



# Conclusions

- Compared to the standard of care, the CAPRI intervention improved RDI, patients' experience, the number and duration of hospitalizations, and the rate of treatment-related grade  $\geq 3$  toxicities.
- This type of intervention should represent a new standard of care in adult patients with cancer receiving oral anti-cancer agents



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