Appendix 1 – Characterization of the SDD studies in MDR-GNB carriers.

Authors	Study	Population	Methods	Results	Limitations
Zuckerman *et al*. 2011[46], Israel	Observational	15 CR-*Kp* carriers with HO disease due for intensive chemotherapy or HSCT	SDD regime: G 80mg qid oral until ES (ES: 3 negative rectal swabs during a 7d window)	ES 10/15 (66%), for an average 9-month period, ES obtained in average 27d; 3/5 NE died from CR- *Kp* BSI; no AE; no resistance development.	No CtG; sample size.
Saidel-Odes *et al*. 2012[36], Israel	RCT	40 hospitalized CR-*Kp* carriers; IG: 20; CtG: 20	SDD: topic gel (Col 100.000 IU/g + G 1,6mg/g) 50mg qid + G oral 80mg qid + Col oral 1 M IU qid, for 7d; CtG: placebo	Decolonization rate at 2 weeks was significantly higher in the IG (61,1%) vs. CtG (16,1%) (OR 0.13; 95% CI 0.02-0.74) but no significant difference at 6 weeks (58,5% IG vs 33,3% CtG); no AE; no resistance development.	Semple restrictions due to exclusion criteria; some treatments in ambulatory due to hospital discharge.
Lubbert et al. 2013, Germany	Retrospective cohort	90 ICU CP-Kp carriers; IG: 14; CtG: 76	SDD: topic gel (Col 100.000 IU/g + G 1,6mg/g) 50mg qid + G oral 80mg qid + Col oral 1 M IU qid, for 7d; CtG: no intervention; ES: 3 negative PCR tests separated by ≥48h	No significant difference on decolonization rate between the 2 groups (43% IG vs. 30% CtG; P=0,102) or on mortality during hospitalization (36% IG vs. 45% CtG; without adequate statistical power); 86% IG with concomitant Ab systemic therapy; 4/14 (28%) developed resistance do SDD agents.	Sample size; majority of IG were elderly with severe co-morbidities.
Oren *et al*. 2013[37], Israel	CT Semi-randomized	152 CRE carriers; CtG: 102; IG: 50 (G 26, Col 16 e GC 8)	SDD 1: G 80mg qid; SDD 2: Col 100mg qid; SDD 3: GC (same doses as previous); CtG: no intervention; SDD until ES or maximum 60d; Rectal swabs every 3d; ES: 3 negative rectal swabs + 1 negative PCR	ES significantly higher in IG (44%) vs. Spontaneous eradication in CtG (7%) (P<0.001), no significant difference between SDD regimes; Average time of SDD: 37 d (10 to 76 d); mortality rate significantly lower in ES group vs. PC group (17% and 49%, respectively; P=0.002); Resistance: 1/16 Col and 6/26 G; no AE.	Not randomized; significant demographic and clinical differences between CtG and IG; no IG follow-up after SDD completion.
Tascini *et al*. 2014[40], Italy	Case series	50 CR-*Kp* carriers, mixed population (elective surgery, chemotherapy, immunosuppression, in-hospital transfer)	SDD: G 80 mg qid, minimum 8d; rectal swabs ever 4d; ES: 2 negative rectal swabs; G plasma measurement on the 3rd d.	ES 34/50 (68%); 6 months follow-up: CR-*Kp* infection 15% ES group vs. 73% NE group; ES 96% with G alone vs. ES 44% with concomitant systemic Ab treatment; no AE.	No CtG; overestimation of ES by culture method and not PCR.
Machuca *et al*. 2016[38], Spain	Restrospective Cohort	77 CP-*Kp* rCol carriers with high infection risk (neutropenia, surgery, previous recurrent CP-*Kp* infections, multiple comorbidities)	SDD 1: G 80mg, qid, oral, 14d; SDD 2: streptomycin 80mg/neomycin 40mg, tid, oral, 14d; CtG: no intervention	180 d follow-up: SDD associated with less mortality risk (HR 0.18; 95% CI 0.06–0.55), less risk of CP-*Kp* infections (HR 0.14; 95% CI 0.02–0.83) and higher microbiological success (HR 4.06; 95% CI1.06–15.6); SDD 1 with less ACM risk (HR 0.15; 95% CI 0.04–0.54), less risk of CP-*Kp* infection (HR 0.86; 95% CI 0.008–0.94) and higher microbiological response (HR 5.67; 95% CI 1.33–24.1); rG 13.6% IG vs. 3% CtG.	Sample size

Appendix 1 - Characterization of the SDD studies in MDR-GNB carriers. (continued)

Authors	Study	Population	Methods	Results	Limitations
De Rosa *et al*. 2017, Italy	Case series	8 hematological allo-HSCT CR-*Kp* carriers	SDD: G 80 mg qid in a 20d window previous to transplant; ES: rectal swab post-treatment with G and follow-up in 6 months	ES 2/8 (25%); 3 patients did not complete the bundle; 1/5 ES and remained negative; 2/4 CR-*Kp* BSI; 2/4 became negative during follow-up; no AE; no resistance development.	No CtG; sample size; incomplete SDD regime information.
Lambelet *et al*. 2017[44], Italy	Case series	14 hematological CR-*Kp* carriers	SDD: G 80 mg qid until 3d after ES; rectal swabs every 3d; ES: 2 negative rectal swabs 48h apart; follow-up 3 months	ES 10/14 (71%); SDD duration: 7 to 25 d; 2/14 rC; 6/14 rFosfomicina; 2/14 rTigeciclina; 4/14 NE, 1 of which was resistant to G and the other 3 had had concomitant systemic Ab treatment; ES: 90% (9/10) with G alone vs. 25% (1/4) with concomitant systemic Ab treatment; no resistance development; no recolonization in 3 months.	No CtG; sample size.
Stoma *et al*. 2018[39], Belarus	RCT	62 HO MR-GN carriers; IG: 31; CtG: 31	SDD: Col 2 M IU, qid oral, 14d; CtG: no intervention	Significant decolonization rate on D14 (61.3% vs. 32.3%; OR 3.32; 95% CI 1.17–9.44; p=0.0241), no significant difference on D21; less BSI incidence in IG on D30 (3.2% vs. 12.9%), but no advantages observed in the overall 90 d of follow-up (*log-rank test*; p=0.4721); no AE; no resistance development to Col.	Not blinded; unicentral study.
Pellicé *et al*. 2021[45], Spain	Observational	73 CP-*Kp* carriers; IG: 52 (26 SDD and 26 SDD+PB); CtG: 21	SDD 1: oral solution 10mL (Col 10mg/ml + Amika 8mg/ml + Nysta 30mg/ml), qid, 10d; SDD 2: SDD 1 followed by PB (Vivomixx®) qd, 20d; CtG: no intervention	1 month follow-up; total ES 76.7%; ES 69.3% taking concomitant Ab therapy vs. 91.6% without concomitant Ab therapy (OR=0.2, 95% CI=0.042–0.99, p=0.04).	Sample size; unicentral study; short follow-up period; ES definition; IG heterogeneity.

Abbreviations: Ab – antibiotic; ACM- all cause mortality; AE – adverse events; Amika – amikacin; BSI – bloodstream infections; CI - confidence interval; Col – colistin; CP-*Kp* – carbapenemase-producing *Klebsiella pneumoniae*; CRE – carbapenem-resistant Enterobacterales; CR-*Kp* – carbapenem-resistant *Klebsiella pneumoniae*; CtG – control group; D – day; ES – eradication status; G – gentamicin; GC - gentamicin + colistin; HCST - hematopoietic stem cell transplantation; HO – hemato-oncological; HR – hazard ratio; IG – intervention group; IU – international units; MDR-GN – multidrug-resistant Gram-negative; M – millions; NE - non eradicated; Nysta – nystatin; OR – odds ratio; PB – probiotic; PC – persistent carriers; PCR - polymerase chain reaction; qd – one time daily; qid – four times daily; rCol – colistin-resistant; RCT – randomized controlled trial; rG – gentamicin-resistant; SDD – selective digestive decontamination; tid – three times daily.