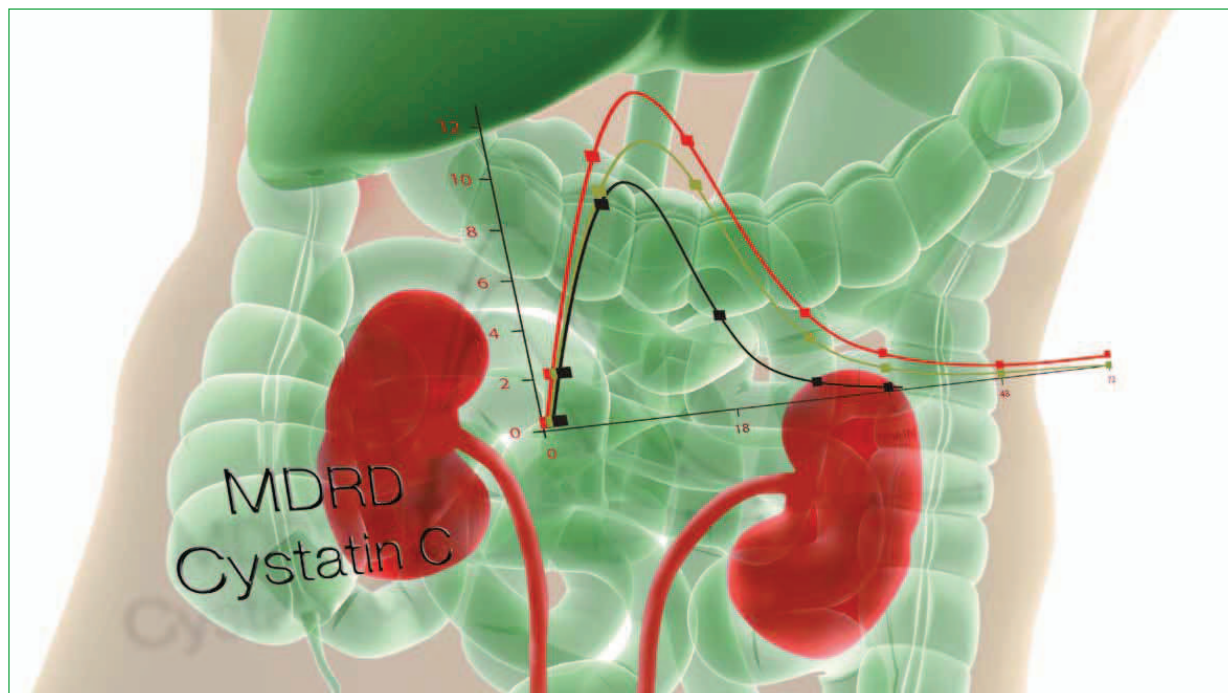


# Your First Address In Europe For Renal Impairment Pharmacokinetics



## Clinical Development Aspects

The current regulatory draft guidances highlight the importance of pharmacokinetic assessments in patients with renal insufficiency in the drug development of NCEs (FDA 2010, EMA 2004). Early phase I/II renal PK investigations are valuable for the conception of later stage trials and with regard to the necessary dosing instructions in the label.

Missing data on renal impairment PK may need justification and can lead to marketing authorisation delays or implementation of contraindications in the SmPC.

## Study Population

The high frequency of comorbidities (e.g. metabolic and cardiovascular) and concomitant medications in renal impairment patients represents a challenge both in terms of recruitment as well as with regard to safety concerns. Investigations in end stage renal disease patients demand well established networks with dialysis units and a high degree of flexibility in the trial set up. Close collaboration with the treating physicians and external experts is the key success factor for a fast and reliable trial conduct.

## Your Advantages At CRS

**Short approval timelines:** 30 days from submission to approval due to CRS's monocentric approach and parallel submission to CA and EC/IRB.

**Fast trial conduct:** Average duration for a single dose trial in renal impaired patients is 4-6 months (screening to last patient out).

**Reliable recruitment:** The close vicinity to the University Medical Centers in Kiel and Lübeck and an intensive cooperation with the treating physicians, several dialysis centres and external specialists enables CRS to provide fast recruitment of suitable patients with well established medical records.

**High standardisation:** CRS's set up allows the mono-centric conduct of complex PK trials with challenging requirements for the study population, avoiding inter-centre variability and guaranteeing highest quality according to phase-I standards.

**Safety:** The infrastructure and expertise enable CRS to work according to the best ethical and medical practice regarding the vulnerable study population.

# High Performance & High Quality In Renal Impaired Patient Trials

## Renal Impairment PK Trials At CRS - A Success Story

Sponsor	Investigational Medicinal Product	Tradenames
Bayer	Rivaroxaban	Xarelto®
Mitsubishi Tanabe	Tenegliptin	Tenelia®
Nycomed	Teduglutide	Revestive®, Gattex®
Novartis	Vildagliptin	Eucreas®, Galvus®
UCB	Lacosamide	Vimpat®

### Trial Design Considerations

For drugs with relevant renal excretion, the regulatory guidances recommend PK studies involving cohorts in all stages of renal impairment (mild, moderate, severe) and matched controls. If administration in patients with end stage renal disease is likely, PK studies in dialysis patients may be required. For narrow therapeutic index drugs (NTID), renal PK studies may be required even in case of small renal excretion rates.

### Accelerate Your Development

The long lasting experience with renal impairment PK trials enables CRS to find individualised strategies and tailored design solutions for a fast and successful development of your product.

### Your Partner In Renal Impairment

CRS is one of the top recruiters worldwide for patients suffering from renal insufficiency, recognised by the authorities and preferred partner by both big pharma and small biotech companies.

Since the early 90s, CRS has realised **more than 120 trials** in patients with renal impairment and is running currently approximately **8 renal impairment trials per year**. All trial concepts are accomplished according to the relevant and effective FDA/EMA guidances and are conducted under highly standardised phase-I conditions - most of them monocentric in own CPUs, specialised in the recruitment and care of patients.

The successful conduct of the trials and the availability of suitable patients are based on the 3 decades of experience of the CPUs lead by internist Dr. Atef Halabi, and on a reliable network with university clinics as well as external medical centres and specialists.

