Low-Dose Radiation Therapy and Severe COVID-19-Related Pneumonia

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Disclosure

• Employment Disclosure: Emory University

• Founder of CureRaysTM, a start-up manufacturer of commercial products to offer COVID-19 treatments with low-dose radiation therapy
RESCUE 1-19 (First LD-RT Trial in the World)

- **Eligible patients** were SARS-CoV-2 positive, hospitalized, bilateral radiographic consolidations & required supplemental oxygen (i.e., severe ARDS)
- **Intervention**: 1.5 Gy whole-lung LD-RT
- **Primary & Secondary Endpoints**: Safety (Phase 1) and Efficacy (Phase 2)
  - **Phase 1** included outcomes in first 5 patients with preplanned interim 7-day analysis (PMID: 32986274)
  - **Phase 2** included outcomes in all 10 patients @ day 28 compared with age- and comorbidity-matched controls.
- **Efficacy endpoints**: time to clinical recovery (TTCR), radiographic improvement on serial x-rays, and biomarkers response
- Two-sample t-tests, chi-square tests, univariate Cox proportional hazard models, cumulative incidences, and hazard ratios were reported.
Results

- Ten patients received whole-lung LD-RT between April 24 and May 24, 2020 and compared with ten matched controls treated with best supportive care and COVID-directed therapies

  - **Primary endpoint**: 7 Day interim

  - **Secondary Endpoints**: Median TTCR was 12 days in controls compared to 3 days in the LD-RT cohort (HR 2.9, p=0.05)

  - Median time to hospital discharge was 20 versus 12 days in LD-RT (p=0.19)

  - Intubation rates were 40% versus 10%, in favor of LD-RT (p=0.12)

  - 28-day overall survival was 90% for both cohorts

  - Age ≥65 was associated with lower oxygen requirement and shorter TTCR in the LD-RT cohort (p=0.01) but not the control cohort (p=0.40)

  - Inflammatory, cardiac, hepatic biomarkers, and serial radiographs also were favored of LD-RT

LD-RT was safe (**PMID: 32986274**)
Observed clinical improvements following LD-RT

**Time to Clinical Recovery**

- Radiation
- Control

\[ P = 0.048 \]

**Time to Hospital Discharge**

- Radiation
- Control

\[ P = 0.19 \]

**Intubation Free Rates**

- Radiation
- Control

\[ P = 0.12 \]
Observed laboratory improvements following LD-RT

**Inflammation**
- C-Reactive Protein:
  - Non-zero change detected: p<0.01
  - Change superior to pre-LDRT levels: p<0.01
  - Change superior to controls (red): p=0.01

**Cardiac Injury**
- Lactate Dehydrogenase:
  - Non-zero change detected: p=0.03
  - Change superior to pre-LDRT levels: p=0.07
  - Change superior to controls (red): p=0.16

**Hepatic Injury**
- Creatine Kinase:
  - Non-zero change detected: p<0.01
  - Change superior to pre-LDRT levels: p=0.45
  - Change superior to controls (red): p=0.08

- Aspartate Aminotransferase (AST):
  - Non-zero change detected: p=0.23
  - Change superior to pre-LDRT levels: p=0.43
  - Change superior to controls (red): p=0.07

- Alanine Aminotransferase (ALT):
  - Non-zero change detected: p=0.22
  - Change superior to pre-LDRT levels: p=0.19
  - Change superior to controls (red): p=0.04
Earlier radiographic improvement following LD-RT

**ARDS Scale Scores - Control Cohort**

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<th>Day 7</th>
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Mean: 3.1 (3.6) 3.3 (3.2) 3.7 (3.4) 3.3 (3.3)

**ARDS Scale Scores - Radiation Cohort**

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Mean: 3.8 3.5 3.3 2.7 (3.1) 2.3 (2.8)

**Contols:** 4 of 7 radiographically improved (57%) p=0.04

**LD-RT:** 9 of 10 radiographically improved (90%)

- First blinded ARDS score decline
- Insufficient radiographs (≤ 1)
Conclusion/Summary

• LD-RT for COVID-19 appears to be safe
• LD-RT seems to improve oxygen status, delirium, radiographs, and biomarkers when compared against age and comorbidity matched cohorts
• Confirmatory trials are needed.
• Clinical Trial Registration: NCT04366791

PrePrints and Pubmed References:
https://www.medrxiv.org/content/10.1101/2020.06.03.20116988v1
https://www.medrxiv.org/content/10.1101/2020.07.11.20147793v1