COVID-19 and Cancer Clinical Trials

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1st Virtual Joint Meeting of NCI Board of Scientific Advisors & National Cancer Advisory Board

April 9, 2020
COVID-19 and Cancer: Some Numbers from Wuhan

- Gender: ~70% male
- Death rate overall: >10%
- ICU admission rate: >15%
- Increased mortality: patients with lung, GI, metastatic cancer

Appreciate the health professionals in cancer centers and in both inpatient and outpatient facilities caring for cancer patients with this virus.
## NCTN Accrual for “Intervention” Step in Trials by Lead Group & Week: 2-3-2020 to 3-29-2020 (CTSU Open Data)

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## NCTN Accrual for “Screening” Step in Trials by Lead Group & Week: 2-3-20 to 3-29-20 (CTSU Open Data)

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COVID-19 and Cancer Clinical Trials

• Some institutions have shut down accrual to most studies; volume of COVID-19 patients has overwhelmed ability to provide care (NYC)

• Several have not: UCSF, NIH clinical center, others: trial accrual continues where staff available to treat those patients:
  ✓ who need curative therapy or who have no viable options beyond a clinical trial
  ✓ with clear potential for therapeutic benefit
  ✓ suggest limiting accrual for non-therapeutic studies
NCI’s Clinical Trials Networks: Response to COVID-19

- Modifications to NCI clinical trial processes
- Tocilizumab compassionate use study
- National COVID-19 natural history study
NCI Adapting to COVID-19 (1)

• Patient care can be transferred to different participating study sites
• Local healthcare providers can provide study activities to provide continuity of care (oversight by responsible investigator)
  ✓ Treatment with non IND drugs
  ✓ Physical exams, KPS, overall assessments
  ✓ Protocol-specific clinical lab tests
  ✓ Protocol-specified blood collections
  ✓ Protocol-specified radiologic imaging, EKG’s, cardiac ultrasound
• NCI can ship oral IND agents directly to patients—including potential to ship multiple cycles of drug; dispensing pharmacies at sites can also ship drugs directly to patients (exceptions for agents considered ‘dangerous goods’ by US Dept. of Transportation; dasatinib, TAK-228, few others)
Injectable CTEP IND agents must be administered at a registered site (FDA).

Alternative procedures that do not compromise safety or the integrity of the study will be considered **minor deviations**:

- Documented in the medical record with reason (i.e., travel restriction)
- Include: study visits by telemedicine rather than in-person; delayed study visits; delayed lab or imaging tests; minimal treatment delays; biospecimen collections

Major deviations may be unavoidable; must still be reported to CIRB.

On-site auditing visits are being re-scheduled; remote auditing has been adopted by NCTN groups.

NCI CIRB supports “remote” informed consent: telephone discussion in conjunction with patient signature on written document.
Compassionate Use Protocol for Tocilizumab

“Tocilizumab in Hospitalized Cancer Patients with Coronavirus 2019 (SARS-CoV-2) And Severe Complications of Corona Virus Disease 19 (COVID-19)”

• NCI will use its treatment referral (compassionate use) mechanism to distribute tocilizumab to cancer patients with incipient respiratory compromise based on potential role of IL-6 in etiology of COVID-19-related ARDS

• Protocol developed by Dr. Rich Little (CTEP) and Dr. Nirali Shah (POB) in 4 days; final negotiations ongoing with Genentech for study to accrue 200 patients (age >2 yrs) with broad eligibility criteria that include severe respiratory compromise from presumed or proven COVID-19 infection. For patients in ICU or about to move to ICU, or worsening lung function in ICU.

• **Goal**: Decrease time in ICU, time on ventilator, time in hospital

• Collect limited clinical data set and blood for biomarker evaluation

• Activate across NCI clinical trials networks in institutions that are not participating in Genentech’s phase III trial of agent
NCI Cancer and COVID-19 Longitudinal Cohort

- NCI building a >2000-patient (sample size estimates ongoing) US national cohort of cancer patients with COVID-19 at > 1000 sites across the NCTN, ETCTN, NCORP, and NCI-designated Cancer Centers to include high, moderate, and currently low prevalence regions; full per case reimbursement from NCI; need to enroll from minority NCORP sites
- NCI infrastructure for development and execution of a natural history study: electronic case report forms, clinical trial documents, banking of blood specimens, NCI CIRB
- Collaborative extramural/NCI leadership team to oversee COVID-19 and Cancer Working Group: clinical trialists, statisticians, epidemiologists, virologists, clinical geneticists, informaticians
- GOALS: 1) Cohort of cancer patients infected with COVID-19 comprising all age groups for collection a comprehensive dataset on the cancers, treatments, medications, symptoms, course, and recovery, and co-morbidities with longitudinal follow-up every 1-2 mo until return to pre-morbid status; 2) Follow subset of pts for > 1 yr to assess impact of COVID-19 on survivorship and QOL; and 3) Collect blood samples at study entry and then every 2 mo for 1 yr to estimate antibody response, genetic susceptibility, and for biomarker development; collect blood from family members; 4) Public database/biospecimens
NCI Cancer and COVID-19 Longitudinal Cohort (2)

Critical Study Milestones:

• Initiate patient accrual before May 15, 2020: from idea to active trial in < 6 weeks
• Enroll the first 500 patients within 3 months of trial activation
• Complete accrual of 2000 patients nationwide by 12/1/2020
• Complete follow-up and survivorship evaluations by end of 2021
• Begin biomarker studies on blood samples soon after initial 500 patients accrued
COVID-19 and Cancer Clinical Trials: Other Critical Activities

- More than a dozen NCI-Designated Cancer Centers have developed their own therapeutic trials for cancer patients with COVID-19
- Vanderbilt CCC initiated a grassroots effort to collect clinical data on cancer patients with COVID-19 infections based on a set of de-identified information; uses an open access, internet database that is now endorsed by >70 Cancer Centers, hospital systems, and large practices: The COVID-19 Cancer Consortium. Opened 3/30/2020
- Large pharma (Roche/Genentech; Amgen; others) has initiated several phase III trials of IL-6R antibodies, antivirals in cancer and non-cancer patients with COVID-19
Appreciation

Demonstrates the potential for NCI—working its grantees—to flexibly make use of its clinical research infrastructure in a time of national emergency

CTEP
Meg Mooney, Larissa Korde, Andrea Denicoff, Rich Little

DCP
Worta McCaskill-Stevens, Paul Pinsky, Marge Good

DCCPS
Robert Croyle, Paul Jacobsen

DCEG
Stephen Chanock

CCR
Bill Dahut, Nirali Shah

Vanderbilt Univ. Comprehensive Cancer Center
Brian Rini, Jeremy Warner
Discussion